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☐ **1: Biotechnology (N Y).** 1992 Oct;10(10):1121-7.

High level expression on a chimeric anti-ganglioside GD2 antibody: genomic kappa sequences improve expression in COS and CHO cells.

Fouser LA, Swanberg SL, Lin BY, Benedict M, Kelleher K, Cumming DA, Riedel GE.

Genetics Institute, Cambridge, Massachusetts 02140.

We report a flexible strategy for the high level expression of a recombinant human monoclonal antibody (mAb) in Chinese hamster ovary (CHO) cells, initially using COS monkey kidney cell transfections to evaluate rapidly modifications to immunoglobulin (Ig) DNA constructs. Using sequential transfections with two amplifiable markers, we generated CHO cell lines and clones that secrete 80-110 micrograms/10(6) cells/24 hours of a mouse-human chimeric IgG1 kappa mAb. This cellular productivity is considerably greater than most murine hybridomas and transfected myelomas. Our data also demonstrate that genomic kappa sequences can improve mAb expression in COS and CHO cells. As a paradigm, we focused our expression studies on a human chimeric form of 3F8, a murine mAb that binds to ganglioside GD2 on neuroblastoma and melanoma tumor cells.

PMID: 1382457 [PubMed - indexed for MEDLINE]

Related Links

Anti-neuroblastoma effec
ch14.18 antibody produ
CHO cells is mediated by
cells in mice; Mol Immunol. ;

On the optimal ratio of h
to light chain genes for
efficient recombinant ant
production; Biochem Biophys Res Commun. ;

Characterization of huma
IgG1 monoclonal antibod

against gangliosides
expressed on *Hydrophilic*
Production and
characterization of a set
mouse-human chimeric
immunoglobulin G (IgG)
subclass and IgA monoclonal
antibodies with identical
variable regions specific for
Pseudomonas aeruginosa
lipopolysaccharide. Immun. 1

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Recombinant antibodies
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DATE: Wednesday, August 23, 2006

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<input type="checkbox"/>	L8	irrelevant same l7	1
<input type="checkbox"/>	L7	heavy\$ same light\$ same (separat\$ or differen\$ or second\$) same expression\$ same vector\$	5421
<input type="checkbox"/>	L6	production\$ and antibod\$ and (two\$ same vector\$ same system\$)	11166
<input type="checkbox"/>	L5	production\$ and antibod\$ and (two\$ smae vector\$ same system\$)	115770
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#31	Search #12 and hybrid cell Limits: Publication Date to 1996/10/10	17:50:52	2
#29	Search #28 and antibody Limits: Publication Date to 1996/10/10	17:50:09	2
#28	Search Trill [author] Limits: Publication Date to 1996/10/10	17:49:56	23
#12	Search heavy and light chain expression vectors in different cells Limits: Publication Date to 1996/10/10	16:47:28	16
#9	Search #1 and #8 Limits: Publication Date to 1996/10/10	16:45:35	19
#8	Search two expression vectors Limits: Publication Date to 1996/10/10	16:45:25	3133
#3	Search #1 and #2 Limits: Publication Date to 1996/10/10	16:43:05	7
#2	Search two vector system Limits: Publication Date to 1996/10/10	16:42:54	1177
#1	Search antibody production Limits: Publication Date to 1996/10/10	16:42:39	49986

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10/719006

MECHANISM OF ACTION - Immunotherapy.

USE - The antibody, its specified portion and variant are useful for treating an immune disease or disorder, e.g. rheumatoid arthritis/seronegative arthropathies, osteoarthritis, or inflammatory bowel disease. (claimed).

Dwg.0/10

L22 ANSWER 9 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-247727 [23] WPIDS

CROSS REFERENCE: 2004-247726 [23]

DOC. NO. CPI: C2004-096685

TITLE: Producing a multi-component **protein**, useful for gene expression or **cell** fusion techniques, comprises fusing recombinant **cells** containing expression cassettes encoding the components of a multimeric **protein**.

DERWENT CLASS: B04 D16

INVENTOR(S): BABCOOK, J; RYLL, T; ZENG, W

PATENT ASSIGNEE(S): (BABC-I) BABCOOK J; (RYLL-I) RYLL T; (ZENG-I) ZENG W; (ABGE-N) ABGENIX INC

COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004053363	A1	20040318	(200423)*		22
WO 2004027043	A2	20040401	(200431)	EN	
RW:	AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE				
	LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE				
	DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE				
	KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO				
	NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ				
	UA UG US UZ VC VN YU ZA ZM ZW				
AU 2003298992	A1	20040408	(200462)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004053363	A1 Cont of	US 2002-247466	20020918
		US 2003-353844	20030128
WO 2004027043	A2	WO 2003-US29869	20030917
AU 2003298992	A1	AU 2003-298992	20030917

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003298992	A1 Based on	WO 2004027043

PRIORITY APPLN. INFO: US 2002-247466 20020918; US
2003-353844 20030128

AN 2004-247727 [23] WPIDS

CR 2004-247726 [23]

AB US2004053363 A UPAB: 20040928

NOVELTY - Producing a multi-component **protein** comprises fusing first and a second recombinant **cells** which contain

Searcher : Shears 571-272-2528

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first and a second expression cassettes containing an amplifiable marker and encoding first and second components of the multimeric **protein** to produce a hybrid **cell** expressing the multimeric **protein**.

DETAILED DESCRIPTION - The method comprises:

(a) introducing a first polynucleotide into a first mammalian **cell**, where the first polynucleotide comprises a first amplifiable marker and a sequence encoding a first component of the multi-component **protein**, the first amplifiable marker is amplifiable by an amplification agent, where the introduction of the **polypeptide** produces a first recombinant **cell**;

(b) introducing a second polynucleotide into a second mammalian **cell**, where the second polynucleotide comprises a second amplifiable marker and a sequence encoding a second component of the multi-component **protein**, the second amplifiable marker is amplifiable by a second amplification agent, where the introduction of the **polypeptide** produces a second recombinant **cell**

;

(c) optionally, repeating (b) for each remaining component of the multi-component **protein**;

(d) fusing **cells** produced from (a)-(c) to form a hybrid **cell**, which expresses the multi-component **protein**;

and

(e) culturing the hybrid **cell** in the presence of the amplification agents for the first and second amplifiable markers, where the first and second recombinant not cultured in the presence of the amplification agents sufficient to provide for amplification of the amplifiable marker until after the fusing.

An INDEPENDENT CLAIM is also included for a method for **producing an antibody**.

USE - The method is useful for producing a multi-component **protein**. The method is useful in gene expression and **cell** fusion techniques.

ADVANTAGE - Amplification of the hybrid, fused **cells** is relatively easier, less time and resource consuming and more efficient than separate amplification of each of the parenteral recombinant **heavy chain** expressing and recombinant **light chain** expressing **cells** prior to fusion. The method also generates a **cell**, which **produces an antibody** at a high rate through the fusion of two kinds of **cells**, which are selected prior to fusion for high **production of the desired heavy or light chains**.

Dwg.0/7

L22 ANSWER 10 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-247726 [23] WPIDS
CROSS REFERENCE: 2004-247727 [23]
DOC. NO. CPI: C2004-096684
TITLE: **Producing a multi-component protein**
 , i.e. an **antibody**, for treating cancer or
 infections, comprises fusing mammalian **cells**
 containing polynucleotides encoding components of the
 protein to form a hybrid **cell**
 expressing the **protein**.
DERWENT CLASS: B04 D16
INVENTOR(S): BABCOOK, J; RYLL, T; ZENG, W
PATENT ASSIGNEE(S): (ABGE-N) ABGENIX INC; (BABC-I) BABCOOK J; (RYLL-I)
 RYLL T; (ZENG-I) ZENG W

Searcher : Shears 571-272-2528

10/719006

COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004053359	A1	20040318	(200423)*		22
AU 2003298992	A1	20040408	(200462)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004053359	A1	US 2002-247466	20020918
AU 2003298992	A1	AU 2003-298992	20030917

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003298992	A1 Based on	WO 2004027043

PRIORITY APPLN. INFO: US 2002-247466 20020918; US
2003-353844 20030128

AN 2004-247726 [23] WPIDS

CR 2004-247727 [23]

AB US2004053359 A UPAB: 20040928

NOVELTY - Producing a multi-component **protein** comprises fusing mammalian **cells** containing polynucleotides encoding components of the multi-component **protein** to form a hybrid **cell** expressing the multi-component **protein**, and culturing the hybrid **cell** in the presence of the amplification agent for the first and second amplifiable markers of the polynucleotides.

DETAILED DESCRIPTION - The method above comprises:

(a) introducing a first polynucleotide into a first mammalian **cell**, where the first polynucleotide comprises a first amplifiable marker and a sequence encoding a first component of the multi-component **protein**, where the first amplifiable marker is amplifiable by an amplification agent;

(b) introducing a second polynucleotide into a second mammalian **cell**, where the second polynucleotide comprises a second amplifiable marker and a sequence encoding a second component of the multi-component **protein**, where the second amplifiable marker is amplifiable by the same amplification agent as the first amplifiable marker;

(c) optionally, repeating step (B) for each remaining component of the multi-component **protein**;

(d) fusing **cells** produced from (A)-(C) to form a hybrid **cell**, which expresses the multi-component **protein**;
and

(e) culturing the hybrid **cell** in the presence of the amplification agent for the first and second amplifiable markers.

An INDEPENDENT CLAIM is also included for a method for producing an **antibody** comprising fusing a first recombinant mammalian **cell** and a second recombinant mammalian **cell** to form a hybrid **cell**, where the first **cell** contains a first polynucleotide comprising a first amplifiable marker and a sequence encoding a **heavy chain polypeptide**, and where the second **cell**

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contains a second polynucleotide comprising a second amplifiable marker and a sequence encoding a **light chain polypeptide**, where the first and second amplifiable markers are amplifiable by the same amplification agent, and culturing the hybrid **cell** in the presence of the amplification agent for the first and second amplifiable markers.

ACTIVITY - Cytostatic; Antibacterial; Immunomodulatory. No biological data given.

MECHANISM OF ACTION - None given.

USE - The methods, polynucleotides, mammalian **cells** and amplifiable markers are useful for **producing** a multimeric **protein**, i.e. an **antibody**, used as therapeutic agents for human disease, such as cancer, microbial infections or disorders of the immune system.

ADVANTAGE - Unlike prior art, the present method generates a **cell** which **produces** an **antibody** at a high rate. Amplification of the hybrid, fused **cell** is relatively easier, less time and resource consuming, and more efficient than separate amplification of each of the parental recombinant **heavy chain-expressing cell** and recombinant **light chain-expressing cell** prior to fusion.

Dwg.0/7

L22 ANSWER 11 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-616322 [60] WPIDS
DOC. NO. CPI: C2004-222064
TITLE: **Producing a protein e.g. a human antibody**, comprises culturing mammalian **cells** introduced separately with polynucleotides encoding **antibody heavy and light chains** and fusing cultured **cells** to form a hybrid **cell** expressing **antibody**.
DERWENT CLASS: B04 D16
INVENTOR(S): DAVIS, C G; GREEN, L; HORI, N; JAKOBOVITS, A; WEBER, R F; ZSEBO, K M
PATENT ASSIGNEE(S): (ABGE-N) ABGENIX INC; (NISB) JAPAN TOBACCO INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
AU 2004200848	A1	20040325	(200460)*		45

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
AU 2004200848	A1	AU 2004-200848	20040303

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2004200848	A1 Div ex	AU 768101

PRIORITY APPLN. INFO: AU 2004-200848 20040303
AN 2004-616322 [60] WPIDS

Searcher : Shears 571-272-2528

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AB AU2004200848 A UPAB: 20040920

NOVELTY - **Producing** (M1) an **antibody**, comprises introducing a polynucleotide encoding a **heavy chain polypeptide** of an **antibody** into a mammalian **cell**, introducing a second polynucleotide encoding a **light chain polypeptide** of the **antibody** into a second mammalian **cell**, culturing each of the **cells** separately and fusing the **produced** cultured **cells** to form a hybrid **cell** expressing **antibody**.

DETAILED DESCRIPTION - **Producing** (M1) an **antibody**, involves (a) introducing a first polynucleotide into a first mammalian **cell**, where the first polynucleotide comprises a first amplifiable marker and a sequence encoding a **heavy chain polypeptide** of an **antibody**, (b) introducing a second polynucleotide into a second mammalian **cell**, where the second polynucleotide comprises a second amplifiable marker and a sequence encoding a **light chain polypeptide** of the **antibody**, (c) culturing each of the first and second **cells** separately in the presence of an amplification agent, where the first and second amplifiable markers are amplified by the same amplification agent, and (d) fusing the cultured **cells produced** by steps (a)-(c) to form a hybrid **cell**, where the hybrid **cells** express the **antibody**. (M1) optionally involves culturing a first recombinant mammalian **cell** in the presence of a first amplification agent to **produce** a first amplified recombinant **cell**, where the first **cell** comprises a first polynucleotide comprising a first amplifiable marker and a sequence encoding a **heavy chain polypeptide**, culturing a second recombinant mammalian **cell** in the presence of a second amplification agent to **produce** a second amplified recombinant **cell**, where the second **cell** comprises a second polynucleotide comprising a second amplifiable marker and a sequence encoding a **light chain polypeptide**, where the first and second amplifiable markers are amplified by the same amplification agent, and fusing the first and second amplified recombinant mammalian **cells** to form a hybrid **cell**, where the hybrid **cell** expressed an **antibody**.

USE - (M1) is useful for **producing** a human **antibody** (claimed).

ADVANTAGE - In (M1), the first **cell** expressing desired **heavy chain** and second **cell** expressing desired **light chain** are selected for one or more desirable characteristics such as high production rate of the heavy or **light chain**, prior to the fusion (claimed).
Dwg.0/10

L22 ANSWER 12 OF 24

MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER: 2004544758 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15459912

TITLE: Comparative proteomic analysis of GS-NS0 murine myeloma **cell** lines with varying recombinant monoclonal **antibody** **production** rate.

AUTHOR: Smales C M; Dinnis D M; Stansfield S H; Alete D; Sage E A; Birch J R; Racher A J; Marshall C T; James D C

CORPORATE SOURCE: Research School of Biosciences, University of Kent,

Searcher : Shears 571-272-2528

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SOURCE: Canterbury, Kent, CT2 7NJ, United Kingdom.
Biotechnology and bioengineering, (2004 Nov 20) 88 (4)
474-88.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041102
Last Updated on STN: 20050422
Entered Medline: 20050421

AB We have employed an inverse engineering strategy based on quantitative proteome analysis to identify changes in intracellular **protein** abundance that correlate with increased specific recombinant monoclonal **antibody production** (qMab) by engineered murine myeloma (NS0) **cells**. Four homogeneous NS0 **cell** lines differing in qMab were isolated from a pool of primary transfectants. The proteome of each stably transfected **cell** line was analyzed at mid-exponential growth phase by two-dimensional gel electrophoresis (2D-PAGE) and individual **protein** spot volume data derived from digitized gel images were compared statistically. To identify changes in **protein** abundance associated with qMab datasets were screened for **proteins** that exhibited either a linear correlation with **cell** line qMab or a conserved change in abundance specific only to the **cell** line with highest qMab. Several **proteins** with altered abundance were identified by mass spectrometry. **Proteins** exhibiting a significant increase in abundance with increasing qMab included molecular chaperones known to interact directly with nascent immunoglobulins during their folding and assembly (e.g., BiP, endoplasmic, **protein** disulfide isomerase). 2D-PAGE analysis showed that in all **cell** lines Mab **light chain** was more abundant than **heavy chain**, indicating that this is a likely prerequisite for efficient Mab production. In summary, these data reveal both the adaptive responses and molecular mechanisms enabling mammalian **cells** in culture to achieve high-level recombinant monoclonal **antibody production**.
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ACCESSION NUMBER: 2003-679629 [64] WPIDS
CROSS REFERENCE: 2003-679625 [64]
DOC. NO. CPI: C2003-185720
TITLE: New nucleic acid, useful for **producing**
humanized or chimeric **antibodies**, or fusion
proteins comprising the **antibodies**,
which are G250-specific and useful for treating
inflammatory conditions, e.g. rheumatoid arthritis or
asthma.
DERWENT CLASS: B04 D16
INVENTOR(S): RENNER, C; SCOTT, A
PATENT ASSIGNEE(S): (LUDW-N) LUDWIG INST CANCER RES
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2003068924 A2 20030821 (200364)* EN 80
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MZ NO NZ OM PH PL
PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN
YU ZA ZM ZW
AU 2003215188 A1 20030904 (200428)
EP 1507859 A2 20050223 (200515) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU
LV MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003068924	A2	WO 2003-US4243	20030212
AU 2003215188	A1	AU 2003-215188	20030212
EP 1507859	A2	EP 2003-711002	20030212
		WO 2003-US4243	20030212

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003215188	A1 Based on	WO 2003068924
EP 1507859	A2 Based on	WO 2003068924

PRIORITY APPLN. INFO: US 2002-355838P 20020213

AN 2003-679629 [64] WPIDS

CR 2003-679625 [64]

AB WO2003068924 A UPAB: 20050303

NOVELTY - An isolated nucleic acid molecule, which encodes a fusion **protein** comprising a chimerized antibody molecule, and a tumor necrosis factor molecule or its fragment, is new. The antibody specifically binds to a target. The fragment of the tumor necrosis factor molecule possesses the **cell** killing properties of a full-length tumor necrosis factor molecule.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a chimeric fusion **protein** encoded by the isolated nucleic acid molecule;

(2) an expression vector comprising the isolated nucleic acid molecule operably linked to a promoter; and

(3) a recombinant **cell** comprising the isolated nucleic acid molecule or the expression vector.

ACTIVITY - Antiinflammatory; Antirheumatic; Antiarthritic; Antipsoriatic; Antiasthmatic; Neuroprotective; Virucide; Antibacterial; Immunosuppressive; Nephrotropic; Antiarteriosclerotic. No biological data given.

MECHANISM OF ACTION - GM-CSF-Antagonist; CD30-Antagonist; G250 Antagonist.

USE - The nucleic acid is useful for the expression of **proteins**, especially **antibodies**, as well as fusion **proteins** that incorporate the **antibody** and a **protein**. The expression vector is useful in **manufacturing** a recombinant **antibody** (e.g. a fully human, humanized or chimeric **antibody**) in a eukaryotic

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cell (claimed). The **antibody** is useful in therapy, particularly for targeting G250 and blocking granulocyte-macrophage stimulating factor (GM-CSF), which is involved in the development of rheumatoid arthritis. The **antibody** is useful for treating inflammatory conditions, e.g. psoriasis, asthma, inflammatory bowel disease, multiple sclerosis, viral or bacterial pneumonia, septic shock, nephritis, or arteriosclerosis.

Dwg.0/5

L22 ANSWER 14 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-430422 [40] WPIDS
DOC. NO. CPI: C2003-113847
TITLE: New nucleic acid molecule useful for producing a heteromeric complex comprises a first nucleic acid operably linked to a second nucleic acid encoding a subunit of a selectable marker .
DERWENT CLASS: B04 D16
INVENTOR(S): BIANCHI, A A; MCGREW, J T
PATENT ASSIGNEE(S): (BIAN-I) BIANCHI A A; (MCGR-I) MCGREW J T; (IMMV) IMMUNEX CORP
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003035887	A1	20030501	(200340)*	EN	28
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
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US 2003082735	A1	20030501	(200340)		
EP 1434871	A1	20040707	(200444)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
AU 2002331883	A1	20030506	(200461)		
JP 2005511031	W	20050428	(200530)		20
MX 2004002489	A1	20050101	(200564)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003035887	A1	WO 2002-US29985	20020920
US 2003082735	A1 Provisional	US 2001-323954P	20010920
		US 2002-251447	20020920
EP 1434871	A1	EP 2002-768877	20020920
		WO 2002-US29985	20020920
AU 2002331883	A1	AU 2002-331883	20020920
JP 2005511031	W	WO 2002-US29985	20020920
		JP 2003-538387	20020920
MX 2004002489	A1	WO 2002-US29985	20020920
		MX 2004-2489	20040316

FILING DETAILS:

PATENT NO	KIND	PATENT NO
	Searcher	: Shears 571-272-2528

10

AN 2003-430422 [40] WPIDS
AB WO2003035887 A UPAB: 20030624

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(3) producing a heteromeric complex.

ADVANTAGE - The invention decreases the time required to select for **cells** expressing high levels of a desired recombinant heteromeric **polypeptide** complex.

L22 ANSWER 15 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-128758 [13] WPIDS
DOC. NO. CPI: C2004-051462
TITLE: New bicistronic expression vector for animal
cells, a transformed cell line
containing the vector and a method for
producing antibody proteins
using them.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): JANG, H S; JUNG, J G; PARK, U Y; RA, G B; SIM, D S;
YANG, J Y; YOO, J S; YOON, H S; CHANG, H S; CHUNG, J
G; PARK, W Y; RAH, G B; SHIM, D S
PATENT ASSIGNEE(S): (GLDS) LG LIFE SCI LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

KR 2003062118	A	20030723 (200413) *	1
KR 450266	B	20040930 (200510)	

PATENT NO	KIND	APPLICATION	DATE
KR 2003062118	A	KR 2002-2544	20020116
KR 450266	B	KR 2002-2544	20020116

Searcher : Shears 571-272-2528

10/719006

PATENT NO	KIND	PATENT NO
KR 450266	B Previous Publ.	KR 2003062118

PRIORITY APPLN. INFO: KR 2002-2544 20020116

AN 2004-128758 [13] WPIDS

AB KR2003062118 A UPAB: 20040223

NOVELTY - A bicistronic expression vector for animal **cells**, a transformed **cell** line containing the same vector and a method for **producing antibody proteins** using the same are provided, effectively expressing various genes such as an antigen gene.

DETAILED DESCRIPTION - A bicistronic expression vector for animal **cells** comprises a cytomegalovirus (CMV) promoter required for **producing** the transcriptional RNA, a foreign gene selected from **light chain** gene or **heavy chain** gene of an **antibody**, an IRES sequence, a selective gene and a poly(A) sequence, sequentially, wherein the selective gene is dihydroxyfolate reductase (DHFR) or neomycin resistance gene (NEOR); the bicistronic expression vector is selected from pLCM-MoK (KCTC 10151BP), pLCD-MoK (KCTC 10151BP), pLCN-MoH (KCTC 10150BP) and pANTIBODY (KCTC 10152BP). A transformed animal **cell** is **produced** by transformation with the bicistronic expression vector. A method for **producing** the foreign gene selected from the **light chain** or **heavy chain** of the **antibody** is characterized by culturing the transformed animal **cell**.
Dwg.1/10

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ACCESSION NUMBER: 2003041514 EMBASE

TITLE: Thyroid-stimulating monoclonal antibodies.

AUTHOR: Sanders J.; Jeffreys J.; Depraetere H.; Richards T.; Evans M.; Kiddie A.; Brereton K.; Groenen M.; Oda Y.; Furmaniak J.; Rees Smith B.

CORPORATE SOURCE: Dr. B. Rees Smith, FIRS Laboratories, RSR Ltd., Parc Ty Glas, Llanishen, Cardiff, CF14 5DU, United Kingdom

SOURCE: Thyroid, (1 Dec 2002) Vol. 12, No. 12, pp. 1043-1050.
Refs: 44

ISSN: 1050-7256 CODEN: THYRER

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology

026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20030207

Last Updated on STN: 20030207

AB Thyrotropin (TSH) receptor monoclonal antibodies (TSHR mAbs) were obtained from cDNA-immunized NMRI mice. Three mAb immunoglobulin Gs (IgGs) (TSMabs 1-3) that had distinct V(H) and V(L) region sequences stimulated cyclic adenosine monophosphate (cAMP) production in isolated porcine thyroid **cells** greater than 10x basal and as little as 20 ng/mL (0.13 nmol/L) of TSMab 1 IgG caused a 2x basal stimulation. TSMab 1 and 2 Fab fragments were also effective stimulators and thyroid-stimulating activities of the IgGs and Fabs were confirmed using TSHR transfected Chinese hamster ovary (CHO)

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cells. The TSmAbs also inhibited (125)I-labeled TSH binding to TSHR-coated tubes by 50% or more at concentrations of 1 µg/mL or less and gave 15%-20% inhibition at 20-50 ng/mL. (125)I-labeled TSmAbs bound to TSHR-coated tubes with high affinity (.apprx.10(10) L/mol) and this binding was inhibited by TSHR autoantibodies with both TSH agonist and antagonist activities. Inhibition of labeled TSmAb binding by Graves' sera correlated well with inhibition of TSH binding ($r = 0.96$; $n = 18$; $p < 0.001$ for TSmAb 2). The TSmAbs have considerable potential as (1) new probes for TSHR structure-function studies, (2) reagents for new assays for TSHR autoantibodies, and (3) alternatives to recombinant TSH in various in vivo applications.

L22 ANSWER 17 OF 24 MEDLINE on STN
ACCESSION NUMBER: 2000418704 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10941907
TITLE: Single-chain antibodies against human insulin-like growth factor I receptor: expression, purification, and effect on tumor growth.
AUTHOR: Li S L; Liang S J; Guo N; Wu A M; Fujita-Yamaguchi Y
CORPORATE SOURCE: Department of Molecular Biology, Beckman Research Institute of the City of Hope, Duarte, CA 91010, USA.
CONTRACT NUMBER: CA65767 (NCI)
SOURCE: Cancer immunology, immunotherapy : CII, (2000 Jul) 49 (4-5) 243-52.
Journal code: 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000905

AB Insulin-like growth factors (IGF) I and II are potent mitogens for a variety of cancer **cells**. The proliferative and anti-apoptotic actions of IGF are mediated by the IGF-I receptor (IGF-IR), to which both IGF-I and IGF-II bind with high affinity. To investigate the mitogenic and anti-apoptotic activities of IGF-IR and to achieve better inhibition of IGF-IR function, single-chain antibodies against human IGF-IR (alphaIGF-IR scFvs) were constructed and expressed. IgG cDNA encoding variable regions of light and **heavy chains** (VL and VH) from mouse IgG were cloned from a hybridoma **producing** the 1H7 alphaIGF-IR monoclonal **antibody** [Li et al., Biochem Biophys Res Commun 196: 92-98 (1993)]. The splice-overlap extension polymerase chain reaction was used to assemble a gene encoding the alphaIGF-IR scFv, including the N-terminal signal **peptide**, VL, linker **peptide**, VH, and C-terminal DYKD tag. Two types of soluble alphaIGF-IR scFvs, a prototype alphaIGF-IR scFv and its alternative type alphaIGF-IR scFv-Fc, were constructed and expressed in murine myeloma **cells**. alphaIGF-IR scFv-Fc, containing the human IgG1 Fc domain, was stably expressed in NS0 myeloma **cells**, using a **glutamine synthase** selection system, and purified from the conditioned medium of stable clones by **protein** -A-agarose chromatography. Levels of alphaIGF-IR scFv-Fc expression ranged from 40 mg/l to 100 mg/l conditioned medium. Sodium dodecyl sulfate/polyacrylamide gel electrophoresis analysis under reducing and nonreducing conditions indicated that alphaIGF-IR scFv-Fc is a dimeric antibody. alphaIGF-IR scFv-Fc retained general characteristics of the

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parental 1H7 monoclonal antibody except that its binding affinity for IGF-IR was estimated to be approximately $10(8) M(-1)$, which was one-order of magnitude lower than that of 1H7 monoclonal antibody. Injection of alphaIGF-IR scFv-Fc (500 microg/mouse, twice a week) significantly suppressed MCF-7 tumor growth in athymic mice. These results suggest that the alphaIGF-IR scFv-Fc is a first-generation recombinant alphaIGF-IR for the potential development of future alphaIGF-IR therapeutics.

L22 ANSWER 18 OF 24 MEDLINE on STN
ACCESSION NUMBER: 1999345930 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10417224
TITLE: Cytogenetic analysis of chimeric **antibody-producing** CHO **cells** in the course of **dihydrofolate reductase**-mediated gene amplification and their stability in the absence of selective pressure.
AUTHOR: Kim S J; Lee G M
CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced Institute of Science and Technology 373-1, Kusong-Dong, Yusong-Gu, Taejon 305-701, Korea.
SOURCE: Biotechnology and bioengineering, (1999 Sep 20) 64 (6) 741-9.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990928
AB Previously, the highest **producing** (HP) recombinant CHO subclones isolated at various methotrexate (MTX) levels showed different **antibody production** stability during long-term culture, although they were clonally derived from CS13 transformant. In this study, genetic basis for their difference in **antibody production** stability was investigated using southern blot hybridization and fluorescence in situ hybridization (FISH) techniques. Southern analysis of HP subclones revealed that **light-chain (LC)** and **heavy-chain (HC)** cDNAs were located closely within 23 kb on an amplification unit, and the configuration of **LC** and **HC** cDNAs within this amplification unit was not disrupted during long-term culture in the absence of MTX. However, when **LC** and **HC** genes were localized on the metaphase chromosomes of HP subclones using FISH, the amplified sequences were present as an extended array on diverse marker chromosomes. HP subclones selected at higher MTX level had more kinds of marker chromosomes. CS13*-002 isolated at 0.02 microM MTX had only one marker chromosome (m002), whereas CS13*-1.0 isolated at 1 microM MTX had five different ones (m10A, m10B, m10C, m10D, and m10E). Each marker chromosome showed different fate during long-term culture of HP subclones in the absence of MTX, resulting in different degrees of stability among the HP subclones. The m10A and m10B remained unchanged, whereas the others disappeared or evolved to variants with shortened amplified arrays. The **cells** containing stable marker chromosomes constituted dominant subpopulations in CS13*-1.0, and thereby CS13*-1.0 became most stable in regard to **antibody**

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production during long-term culture. Furthermore, our dual-color FISH showed that the telomeric ends of amplified arrays on the stable marker chromosomes were always surrounded by (TTAGGG)(n) sequences, indicating that (TTAGGG)(n) sequences are closely related to the stability and evolution of amplified sequences. Taken together, our data show that the assessment of genotypic stability of amplified CHO **cells** is a prerequisite for understanding their production stability during long-term culture in the absence of selection pressure.

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L22 ANSWER 19 OF 24 MEDLINE on STN
 ACCESSION NUMBER: 1999290079 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10361728
 TITLE: Changes during subclone development and ageing of human **antibody-producing** recombinant CHO **cells**.
 AUTHOR: Strutzenberger K; Borth N; Kunert R; Steinfeldner W; Katinger H
 CORPORATE SOURCE: Institute for Applied Microbiology, University of Agriculture, Vienna, Austria.
 SOURCE: Journal of biotechnology, (1999 Apr 15) 69 (2-3) 215-26.
 Journal code: 8411927. ISSN: 0168-1656.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199907
 ENTRY DATE: Entered STN: 19990730
 Last Updated on STN: 19990730
 Entered Medline: 19990719

AB Some of the problems encountered with human or human-mouse heterohybridomas, such as low growth rates and high serum requirements, have led to the increased use of recombinant **cell** lines for **production** of human **antibodies**. To evaluate the suitability of such alternative **cell** lines for the **production** of human **antibodies** we have analysed several subclones with differing specific **production** rates of a recombinant CHO **cell** line. Gene copy number and site of chromosomal integration for the light and **heavy chain** and the **dhfr** gene were determined by in-situ hybridisation. Specific mRNA content was analysed by Northern blot. In addition the intracellular content in light and **heavy chain** was measured by flow cytometry and the specific secretion rates were determined. The stability of gene expression was followed in the highest producing subclone for over a year. As previously seen in heterohybridoma **cells** a high expression rate of **light chain** is beneficial in speeding up secretion rates of whole antibody. When grown in the presence of G418 and methotrexate the amplified gene copies in the genome of recombinant CHO **cells** were stable over more than 100 passages. However, the expression of **light chain**, and with it the secretion rate, decreased with time. The low intracellular concentration of **light chain** resulted in accumulation of **heavy chain** in the endoplasmic reticulum due to retention by chaperones. The specific secretion rate decreased by 50% after 100 passages. When no G418 or methotrexate were present 75% of the gene copies were lost after 100

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passages.

L22 ANSWER 20 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-251296 [22] WPIDS
DOC. NO. CPI: C1998-078411
TITLE: **Production of multi-component
proteins, particularly antibodies -
by fusing cells which contain nucleotide
sequences encoding each of the components of the
multi-component protein.**
DERWENT CLASS: B04 D16
INVENTOR(S): DAVIS, C G; GREEN, L; HORI, N; JAKOBOVITS, A; WEBER,
R F; ZSEBO, K M
PATENT ASSIGNEE(S): (ABGE-N) ABGENIX INC; (NISB) JAPAN TOBACCO INC;
(ABGE-N) AVGENIX INC; (DAVI-I) DAVIS C G; (HORI-I)
HORI N; (JAKO-I) JAKOBOVITS A; (ZSEB-I) ZSEBO K M
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9816654	A1	19980423	(199822)*	EN	44
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9749898	A	19980511	(199837)		
US 5916771	A	19990629	(199932)		
EP 931162	A1	19990728	(199934)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
KR 2000049053	A	20000725	(200116)		
US 6207418	B1	20010327	(200119)		
JP 2001505049	W	20010417	(200128)		48
AU 734800	B	20010621	(200141)		
AU 2001072174	A	20011220	(200208)#		
US 2002076763	A1	20020620	(200244)		
US 6420140	B1	20020716	(200254)		
US 2002098551	A1	20020725	(200256)#		
US 2003022291	A1	20030130	(200311)		
AU 768101	B	20031204	(200382)#		
US 6677138	B2	20040113	(200405)		
KR 416680	B	20040131	(200428)		
US 2004142430	A1	20040722	(200449)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9816654	A1	WO 1997-US18910	19971010
AU 9749898	A	AU 1997-49898	19971010
US 5916771	A	US 1996-730639	19961011
EP 931162	A1	EP 1997-912801	19971010
		WO 1997-US18910	19971010
KR 2000049053	A	WO 1997-US18910	19971010
		KR 1999-703123	19990410
US 6207418	B1 Cont of	US 1996-730639	19961011
		US 1999-342301	19990629

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JP 2001505049	W		WO 1997-US18910	19971010
			JP 1998-518642	19971010
AU 734800	B		AU 1997-49898	19971010
AU 2001072174	A	Div ex	AU 1997-49898	19971010
			AU 2001-72174	20010918
US 2002076763	A1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
			US 2001-945387	20010830
US 6420140	B1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
			US 2001-769070	20010124
US 2002098551	A1		US 2001-769070	20010124
US 2003022291	A1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
		Cont of	US 2001-945387	20010830
			US 2002-155839	20020524
AU 768101	B	Div ex	AU 1997-49898	19971010
			AU 2001-72174	20010918
US 6677138	B2	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
			US 2001-945387	20010830
KR 416680	B		WO 1997-US18910	19971010
			KR 1999-703123	19990410
US 2004142430	A1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
		Cont of	US 2001-945387	20010830
			US 2003-719006	20031120

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9749898	A Based on	WO 9816654
EP 931162	A1 Based on	WO 9816654
KR 2000049053	A Based on	WO 9816654
US 6207418	B1 Cont of	US 5916771
JP 2001505049	W Based on	WO 9816654
AU 734800	B Previous Publ. Based on	AU 9749898 WO 9816654
AU 2001072174	A Div ex	AU 734800
US 6420140	B1 Cont of	US 5916771
	Cont of	US 6207418
US 2003022291	A1 Cont of	US 5916771
	Cont of	US 6207418
	Cont of	US 6420140
AU 768101	B Previous Publ. Div ex	AU 2001072174 AU 734800
US 6677138	B2 Cont of	US 5916771
	Cont of	US 6207418
	Cont of	US 6420140
KR 416680	B Previous Publ. Based on	KR 2000049053 WO 9816654
US 2004142430	A1 Cont of	US 5916771
	Cont of	US 6207418
	Cont of	US 6420140

Searcher : Shears 571-272-2528

Cont of

US 6677138

PRIORITY APPLN. INFO: US 1996-730639 19961011; US
 1999-342301 19990629; AU
 2001-72174 20010918; US
 2001-769070 20010124; US
 2001-945387 20010830; US
 2002-155839 20020524; US
 2003-719006 20031120

AN 1998-251296 [22] WPIDS

AB WO 9816654 A UPAB: 19980604

A method (A) for **producing** a multi-component **protein** (MCP) comprises: (a) introducing a first nucleotide sequence (NS) into a first **cell**, where the first NS encodes a first component of the MCP; (b) introducing a second NS into a second **cell**, where the second NS encodes a second component of the MCP; (c) optionally repeating step (b) for each remaining component of the MCP, and (d) fusing **cells produced** from steps (a)-(c) to form a hybrid **cell**, whereby the hybrid **cell** expresses the MCP. Also claimed is a method (B) for screening for successful fusion of a first **cell** containing a first NS encoding a desired **antibody heavy chain** and a second **cell** containing a second NS encoding a desired **antibody light chain**, comprising: (a) including a NS encoding a first marker gene in the first **cell**; (b) including a NS encoding a second marker gene in the second **cell**; (c) fusing the first **cell** and the second **cell** under fuseogenic conditions to **produce** a fused **cell**, and (d) assaying for the presence of the first and second marker genes in the fused **cell**, whereby detection of the presence of the first and second marker genes in the fused **cell** indicates a successful fusion. Also claimed is a multi-component **protein produced** as in (A).

The marker genes are preferably the hygromycin resistance gene, the neomycin resistance (neo) gene, the hypoxanthine phosphoribosyl transferase gene, the **dihydrofolate reductase** (**DHFR**) gene, and the LacZ reporter gene. The method further comprises: (e) culturing the hybrid **cells** so as to express the multi-component **protein**, and (f) recovering the multi-component **protein** from the hybrid **cell** culture. The first and second **cells** are selected from mammalian, myeloma and non-lymphoid **cells**. The **protein** is an antibody.

USE - The method allows separately transformed **cells** to be individually selected for optimal expression of each component of the MCP. The method results in a final MCP product which is not expressed until a single hybrid **cell** is produced from the fusion of each **cell** expressing a component of the final **protein** product.

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L22 ANSWER 21 OF 24 MEDLINE on STN
 ACCESSION NUMBER: 1999201274 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10099478
 TITLE: Clonal variability within **dihydrofolate reductase**-mediated gene amplified Chinese hamster ovary **cells**: stability in the absence of selective pressure.
 AUTHOR: Kim N S; Kim S J; Lee G M

Searcher : Shears 571-272-2528

10/719006

CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced
Institute of Science and Technology 373-1, Kusong-Dong,
Yusong-Gu, Taejon 305-701, Korea.
SOURCE: Biotechnology and bioengineering, (1998 Dec 20) 60 (6)
679-88.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990517

AB Recombinant Chinese hamster ovary (rCHO) **cells** expressing a
high level of chimeric antibody were obtained by cotransfection of
heavy- and **light-chain** cDNA expression vectors
into **dihydrofolate reductase**-deficient CHO
cells and subsequent gene amplification in medium containing
stepwise increments in methotrexate (MTX) level up to 1.0 microM. To
determine the clonal variability within the amplified **cell**
population in regard to **antibody production**
stability, 20 subclones were randomly isolated from the amplified
cell population at 1.0 microM MTX (CS13-1.0 **cells**).
Clonal analysis showed that CS13-1.0 **cells** were
heterogeneous with regard to specific growth rate (μ) and specific
antibody productivity (qAb), although they were derived from a single
clone. The μ and qAb of 20 subclones were in the range of 0.51 to
0.72 day⁻¹ and 10.9 to 19.1 microgram/10(6) **cells**/day,
respectively. During 8 weeks of cultivation in the absence of
selective pressure, the μ of most subclones did not change
significantly. On the other hand, their qAb decreased significantly.
Furthermore, the relative decrease in qAb varied among subclones,
ranging from 30% to 80%. Southern and Northern blot analyses showed
that this decreased qAb resulted mainly from the loss of amplified
immunoglobulin (Ig) gene copies and their respective cytoplasmic
mRNAs. For the sake of screening convenience, an attempted was made
to correlate the initial properties of subclones (such as μ , qAb, and
Ig gene copies) with their **antibody production**
stability during long-term culture. Among these initial properties
examined, only qAb of subclones could help to predict their stability
to some extent. The subclones with high qAb were relatively stable
with regard to **antibody production** during
long-term culture in the absence of selective pressure ($P < 0.005$,
ANOVA). Taken together, the clonal heterogeneity in an amplified CHO
cell population necessitates clonal analysis for screening
stable clones with high qAb.
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L22 ANSWER 22 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation
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ACCESSION NUMBER: 1997:130865 BIOSIS
DOCUMENT NUMBER: PREV199799422678
TITLE: Comparison of the **production** of a human
monoclonal **antibody** against HIV-1 by
heterohybridoma **cells** and recombinant CHO
cells: A flow cytometric study.
AUTHOR(S): Borth, Nicole [Reprint author]; Strutzenberger, Karl;
Donalies, Ute; Kunert, Renate; Katinger, Hermann

Searcher : Shears 571-272-2528

10/719006

CORPORATE SOURCE: Inst. Applied Microbiol., Nussdorfer Laende 11, 1190
Vienna, Austria
SOURCE: Cytotechnology, (1996) Vol. 22, No. 1-3, pp. 129-138.
ISSN: 0920-9069.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Mar 1997
Last Updated on STN: 25 Mar 1997

AB The **production** of human monoclonal **antibodies** for therapeutic use is of increasing importance for treatment of viral infections such as AIDS. As human x mouse heterohybridomas rarely reach the growth rates and **cell** specific production rates of mouse hybridomas the transfection of standard **cell** lines, such as CHO or BHK, is a promising alternative. This has the additional advantage that the IgG subtype can be changed to suit the desired application. However, the use of a **cell** line that has not originally developed to **produce antibodies**, as lymphocytes and myeloma **cells** have, might have unrecognised drawbacks. This will be especially significant in the case of antibodies as each molecule consists of 4 chains linked by disulphide bonds which require specific intracellular factors to be properly folded and processed (**Heavy chain binding protein, Protein Disulfide Isomerase a.o.**). In this study we have therefore compared two **cell** lines: a human x mouse heterohybridoma **producing** IAM-2F5, a human IgG-3 **antibody** specific for HIV-1 with neutralising properties and a Chinese Hamster Ovary **cell** transfected with **dihydrofolate reductase** and with the heavy and **light chain** genes of IAM-2F5 modified to IgG-1. From each **cell** line three subclones were selected with low, medium and high specific production rates. Batch cultures were performed and the following cellular parameters analysed by flow cytometry; 1) total RNA content (translational activity); 2) total **protein** content; 3) **cell** cycle phase distribution; 4) concentration of light and **heavy chains**; 5) concentration of helper **proteins** such as BiP and PDI. The production rate of heterohybridoma **cells** was best reflected in the intracellular concentration of kappa chain, while the gamma chain concentration was comparable for all three subclones. In the CHO **cells** the gamma chain expression and thus gene copy number appeared to be the limiting factor. The GRP78/BiP concentration in CHO remained unchanged in spite of a 5-fold higher concentration of gamma chain in the high producing subclone. The PDI concentration in CHO **cells** was much lower compared to the heterohybridoma **cells**, irrespective of production rates.

L22 ANSWER 23 OF 24 MEDLINE on STN
ACCESSION NUMBER: 94141203 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8308283
TITLE: A new vector for the high level expression of chimeric antibodies in myeloma **cells**.
AUTHOR: Shitara K; Nakamura K; Tokutake-Tanaka Y; Fukushima M; Hanai N
CORPORATE SOURCE: Division of Immunology, Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Japan.
SOURCE: Journal of immunological methods, (1994 Jan 3) 167 (1-2) 271-8.
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands

Searcher : Shears 571-272-2528

10/719006

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19970203
Entered Medline: 19940311

AB We previously reported the expression of a mouse/human chimeric anti-ganglioside GD3 antibody, KM871 (IgG1,kappa) in mouse myeloma SP2/0 **cells** under the control of the ecotropic Moloney virus long terminal repeat by the co-transfection of chimeric heavy (H) and light (L) chain vectors (Shitara et al. (1993) Cancer Immunol. Immunother.). To establish an efficient and high level expression system for the chimeric antibody, we did comparative study on vector systems and host **cells**. An improved expression vector, named 'a tandem vector, pChi641HLGM4' was constructed, in which both of the chimeric H and L chain gene transcription units and a **dihydrofolate reductase (dhfr)** gene transcription unit were inserted. When two kinds of mouse myeloma **cell** lines, SP2/0 and P3U1, were used as host **cells**, frequency of the incidence of **antibody-producing** transfectants was markedly increased by the use of the tandem vector compared with the use of the mixture of each chimeric H vector and L chain vector. To select out appropriate host **cells**, transfection frequency and **antibody production** level were compared among SP2/0, P3U1 and rat myeloma YB2/0 **cells** by transfection of the tandem vector. YB2/0 **cell** was shown to have the highest potential in both the transfection frequency and the **antibody production**. Introduction of the tandem vector into YB2/0 **cells** and the subsequent amplification with 50-200 nM methotrexate gave rise to several clones that stably secreted 70-100 micrograms/10(6) **cells** per 24 h of the chimeric antibody. This productivity of the antibody is one of the highest levels which have been achieved by other investigators using transfected myeloma **cells**. Using this system it took only 2-3 months to establish the transfectant clones which stably **produced** the chimeric **antibody**.

L22 ANSWER 24 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 87116049 EMBASE
DOCUMENT NUMBER: 1987116049
TITLE: Reconstitution of functionally active antibody directed against creatine kinase from separately expressed heavy and **light chains** in non-lymphoid **cells**.
AUTHOR: Weidle U.H.; Borgya A.; Mattes R.; et al.
CORPORATE SOURCE: Boehringer Mannheim GmbH, Biochemical Research Center, D-8132 Tutzing, Germany
SOURCE: Gene, (1987) Vol. 51, No. 1, pp. 21-29.
CODEN: GENED6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211

Searcher : Shears 571-272-2528

10/719006

AB We report here for the first time reconstitution and secretion and functionally active antibody in non-lymphoid **cells**. Expression vectors for the light and the **heavy chain** of a monoclonal antibody directed against creatine kinase (EC 2.7.3.2) were introduced into COS and CHO Chinese hamster ovary **dhfr-cells**. Introduction of the expression vectors separately gave rise to immuno-reactive material in the culture supernatants, but only cotransfection of the expression plasmids resulted in secretion of **protein** with immuno-reactivity against antibodies directed against mouse heavy and **light chains** as well as specific antigen-binding affinity, as determined by enzyme-linked immunosorbent assay. Secreted κ and γ chains from reconstituted antibody were characterized by immunoadsorption and sodium dodecyl sulfate-polyacrylamide gel electrophoresis. In COS **cells**, reconstituted antibody was transiently secreted; cotransfection of κ and γ chain expression plasmids with a **dihydrofolate reductase (DHFR)**-expression plasmid into CHO **dhfr-cells** gave rise to stable transformants secreting functionally active antibody.

FILE 'MEDLINE' ENTERED AT 17:01:27 ON 11 JAN 2006

FILE LAST UPDATED: 10 JAN 2006 (20060110/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

L23	64412	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTIBODIES/CT
L24	4652	SEA FILE=MEDLINE ABB=ON	PLU=ON	"ADENOSINE DEAMINASE"/CT
L25	4007	SEA FILE=MEDLINE ABB=ON	PLU=ON	"TETRAHYDROFOLATE DEHYDROGENASE"/CT
L26	34	SEA FILE=MEDLINE ABB=ON	PLU=ON	L23 AND (L24 OR L25)
L27	4276	SEA FILE=MEDLINE ABB=ON	PLU=ON	CELLS/CT
L28	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	L26 AND L27
L23	64412	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTIBODIES/CT
L24	4652	SEA FILE=MEDLINE ABB=ON	PLU=ON	"ADENOSINE DEAMINASE"/CT
L25	4007	SEA FILE=MEDLINE ABB=ON	PLU=ON	"TETRAHYDROFOLATE DEHYDROGENASE"/CT
L26	34	SEA FILE=MEDLINE ABB=ON	PLU=ON	L23 AND (L24 OR L25)
L29	118802	SEA FILE=MEDLINE ABB=ON	PLU=ON	PROTEINS/CT
L30	84572	SEA FILE=MEDLINE ABB=ON	PLU=ON	PEPTIDES/CT
L31	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	L26 AND (L29 OR L30)

Searcher : Shears 571-272-2528

10/719006

L31 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 95349954 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7624146
TITLE: Preferential detection of catalytically inactive
c-erbB-2 by antibodies to unphosphorylated peptides
mimicking receptor tyrosine autophosphorylation sites.
AUTHOR: Epstein R J
CORPORATE SOURCE: Division of Cell, Molecular and Oncology Research,
Charing Cross & Westminster Medical School, University
of London, UK.
SOURCE: Oncogene, (1995 Jul 20) 11 (2) 315-23.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950911
Last Updated on STN: 20000303
Entered Medline: 19950831
ED Entered STN: 19950911
Last Updated on STN: 20000303
Entered Medline: 19950831
AB The c-erbB-2 tyrosine kinase is often overexpressed in human breast
cancer, but correlations of receptor expression with tumour behaviour
have proven elusive in patients without metastases at diagnosis. To
address the possibility that receptor function may be more informative
than expression, we previously developed function-specific c-erbB-2
antibodies using synthetic tyrosine-phosphorylated peptide immunogens
(Epstein et al., Proc. Natl. Acad. Sci. USA 1992; 89:
10435-10439). Here the converse approach has been taken to determine
the functional status of c-erbB-2 receptors detected by antibodies to
dephosphorylated (dep) autophosphorylation sequences. In contrast to
antiphosphopeptide (apt) antibodies, dep antibodies to the Tyr1248
autophosphorylation site exhibited preferential, but not exclusive,
binding to tyrosine-dephosphorylated c-erbB-2. Consistent with this,
catalytically active and inactive receptors could not be clearly
distinguished by in vitro autophosphorylation experiments in which
c-erbB-2 was immunoprecipitated using a monoclonal Tyr1248 dep
antibody. A dep antiserum recognizing autophosphorylation sites
N-terminal to Tyr1248 exclusively recognized tyrosine-dephosphorylated
c-erbB-2 following antibody preabsorption with homologous
phosphopeptides. Although indirect, these data are consistent with a
model of sequential c-erbB-2 autophosphorylation in which Tyr1248 is
the final residue modified. Moreover, since many studies of c-erbB-2
expression have used antibodies to dephosphorylated
autophosphorylation sites, these results caution against automatically
equating such receptor immunoreactivity with in vivo function or
clinical significance.

FILE 'HOME' ENTERED AT 17:05:59 ON 11 JAN 2006

10/719006

=> d his ful

(FILE 'HOME' ENTERED AT 16:39:00 ON 11 JAN 2006)
DEL HIS Y

FILE 'REGISTRY' ENTERED AT 16:43:41 ON 11 JAN 2006

E DIHYDROFOLATE REDUCTASE/CN 5
L1 268 SEA ABB=ON PLU=ON DIHYDROFOLATE REDUCTASE?/CN
E GLUTAMINE SYNTHASE/CN 5
L2 17 SEA ABB=ON PLU=ON GLUTAMINE SYNTHASE?/CN
E ADENOSINE DEAMINASE/CN 5
L3 123 SEA ABB=ON PLU=ON ADENOSINE DEAMINASE?/CN
L4 408 SEA ABB=ON PLU=ON L1 OR L2 OR L3

FILE 'HCAPLUS' ENTERED AT 16:44:35 ON 11 JAN 2006

L5 37197 SEA ABB=ON PLU=ON L4 OR DHFR OR GS OR (DIHYDROFOLATE OR
DI(W) (HYDROFOLATE OR HYDRO FOLATE) OR DIHYDRO FOLATE) (W) (RE
DUCTASE OR DEHYDROGENASE OR DE HYDROGENASE) OR GLUTAMINE
SYNTHASE OR ADENOSINE (W) (DEAMINASE OR DE AMINASE OR
AMINOHYDROLASE OR AMINO HYDROLASE)
L6 831 SEA ABB=ON PLU=ON (TETRAHYDROFOLATE OR TETRA(W) (HYDROFOLA
TE OR HYDRO FOLATE) OR TETRAHYDRO FOLATE) (W) (DEHYDROGENASE
OR DE HYDROGENASE) OR FOLIC (1W) REDUCTASE
L7 2000 SEA ABB=ON PLU=ON (L5 OR L6) AND ANTIBOD?
D QUE
L8 144 SEA ABB=ON PLU=ON L7 AND (LIGHT CHAIN OR LC)
L9 99 SEA ABB=ON PLU=ON L8 AND (HEAVY CHAIN OR HC)
L10 93 SEA ABB=ON PLU=ON L9 AND CELL
L11 6 SEA ABB=ON PLU=ON L9 AND (MYELOMA OR NSO OR NSO OR
HYBRID) (3A) CELL
D KWIC
L12 40 SEA ABB=ON PLU=ON L10 AND (PRODUCING OR PRODUCE# OR
PRODUCTION OR MANUF?)
L13 0 SEA ABB=ON PLU=ON L12 AND (POLYNUCLEOTIDE OR POLY
NUCLEOTIDE)
L14 31 SEA ABB=ON PLU=ON L12 AND (POLYPEPTIDE OR POLYPROTEIN OR
PROTEIN OR PEPTIDE)
D QUE
L*** DEL 90515 S (PRODUCING OR PRODUCE# OR PRODUCTION OR MANUF?) (L) ANTIBOD
D KWIC
L*** DEL 419 S L15 AND (L5 OR L6)
L*** DEL 40 S L12 AND (LIGHT CHAIN OR LC)
L*** DEL 50 S L16 AND (LIGHT CHAIN OR LC)
L*** DEL 48 S L16 AND (HEAVY CHAIN OR HC)
L*** DEL 40 S L17 AND (HEAVY CHAIN OR HC)
L*** DEL 39 S L18 AND CELL
D KWIC
D KWIC 2
L15 52430 SEA ABB=ON PLU=ON (PRODUCING OR PRODUCE# OR PRODUCTION
OR MANUF?) (S) ANTIBOD?
D KWIC
L16 257 SEA ABB=ON PLU=ON L15 AND (L5 OR L6 OR GLUTAMINE
SYNTHETASE)
L17 46 SEA ABB=ON PLU=ON L16 AND (LIGHT CHAIN OR LC)
L18 38 SEA ABB=ON PLU=ON L17 AND (HEAVY CHAIN OR HC)
D QUE
D KWIC
L19 37 SEA ABB=ON PLU=ON L18 AND CELL
D KWIC

Searcher : Shears 571-272-2528

10/719006

D KWIC 2
D KWIC 3
D QUE
L20 28 SEA ABB=ON PLU=ON L19 AND (POLYPROTEIN OR POLYPEPTIDE OR
PEPTIDE OR PROTEIN)
L*** DEL 0 S L20 AND HORI ?/AU
L*** DEL 0 S L20 AND DAVIS ?/AU
L*** DEL 1 S (HORI ? AND DAVIS ?)/AU
D TI AU
D .BEVSTR1

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
JICST-EPLUS, JAPIO' ENTERED AT 16:57:46 ON 11 JAN 2006
L21 30 SEA ABB=ON PLU=ON L20
L22 24 DUP REM L21 (6 DUPLICATES REMOVED)

FILE 'REGISTRY' ENTERED AT 17:01:15 ON 11 JAN 2006

FILE 'HCAPLUS' ENTERED AT 17:01:15 ON 11 JAN 2006
D QUE L20
D L20 1-28 .BEVSTR

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
JICST-EPLUS, JAPIO' ENTERED AT 17:01:20 ON 11 JAN 2006
D L22 1-24 IBIB ABS

FILE 'MEDLINE' ENTERED AT 17:01:27 ON 11 JAN 2006
E ANTIBODIES/CT 5
L23 64412 SEA ABB=ON PLU=ON ANTIBODIES/CT
E ADENOSINE DEAMINASE/CT 5
L24 4652 SEA ABB=ON PLU=ON "ADENOSINE DEAMINASE"/CT
E GLUTAMINE SYNTHASE/CT 5
E TETRAHYDROFOLATE DEHYDROGENASE/CT 5
L25 4007 SEA ABB=ON PLU=ON "TETRAHYDROFOLATE DEHYDROGENASE"/CT
L26 34 SEA ABB=ON PLU=ON L23 AND (L24 OR L25)
E CELLS/CT 5
L27 4276 SEA ABB=ON PLU=ON CELLS/CT
L28 0 SEA ABB=ON PLU=ON L26 AND L27
E POLYPEPTIDES/CT 5
E POLYPEPTIDE/CT 5
E POLYPROTEIN/CT 5
E PROTEINS/CT 5
L29 118802 SEA ABB=ON PLU=ON PROTEINS/CT
E PEPTIDES/CT 5
L30 84572 SEA ABB=ON PLU=ON PEPTIDES/CT
L31 1 SEA ABB=ON PLU=ON L26 AND (L29 OR L30)
D QUE L28
D QUE L31
D L31 .BEVERLYMED

FILE 'HOME' ENTERED AT 17:05:59 ON 11 JAN 2006

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JAN 2006 HIGHEST RN 871658-99-0
DICTIONARY FILE UPDATES: 10 JAN 2006 HIGHEST RN 871658-99-0

Searcher : Shears 571-272-2528

10/719006

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information.  *
*
*****
```

Structure search iteration limits have been increased. See HELP SLIMI
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCAPLUS

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FILE COVERS 1907 - 11 Jan 2006 VOL 144 ISS 3
FILE LAST UPDATED: 10 Jan 2006 (20060110/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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FILE MEDLINE

FILE LAST UPDATED: 10 JAN 2006 (20060110/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details
on the 2005 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht

Searcher : Shears 571-272-2528

10/719006

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 4 January 2006 (20060104/ED)

FILE EMBASE

FILE COVERS 1974 TO 6 Jan 2006 (20060106/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE WPIDS

FILE LAST UPDATED: 6 JAN 2006 <20060106/UP>

MOST RECENT DERWENT UPDATE: 200602 <200602/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

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GUIDES, PLEASE VISIT:

<http://scientific.thomson.com/support/products/dwpi/>

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.

FOR FURTHER DETAILS:

<http://scientific.thomson.com/support/products/dwpifv/>

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
PLEASE CHECK:

<http://scientific.thomson.com/support/patents/dwpieref/reftools/classif>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html <

FILE CONFSCI

FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

10/719006

FILE SCISEARCH

FILE COVERS 1974 TO 4 Jan 2006 (20060104/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS

FILE COVERS 1985 TO 10 JAN 2006 (20060110/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO

FILE LAST UPDATED: 02 JAN 2006 <20060102/UP>

FILE COVERS APR 1973 TO SEPTEMBER 29, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html <

FILE HOME

10/719006

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FILE COVERS 1907 - 11 Jan 2006 VOL 144 ISS 3
FILE LAST UPDATED: 10 Jan 2006 (20060110/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

L1 268 SEA FILE=REGISTRY ABB=ON PLU=ON DIHYDROFOLATE REDUCTASE?/
CN
L2 17 SEA FILE=REGISTRY ABB=ON PLU=ON GLUTAMINE SYNTHASE?/CN
L3 123 SEA FILE=REGISTRY ABB=ON PLU=ON ADENOSINE DEAMINASE?/CN
L4 408 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L2 OR L3
L5 37197 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 OR DHFR OR GS OR
(DIHYDROFOLATE OR DI(W) (HYDROFOLATE OR HYDRO FOLATE) OR
DIHYDRO FOLATE) (W) (REDUCTASE OR DEHYDROGENASE OR DE
HYDROGENASE) OR GLUTAMINE SYNTHASE OR ADENOSINE(W) (DEAMINAS
E OR DE AMINASE OR AMINOHYDROLASE OR AMINO HYDROLASE)
L6 831 SEA FILE=HCAPLUS ABB=ON PLU=ON (TETRAHYDROFOLATE OR
TETRA(W) (HYDROFOLATE OR HYDRO FOLATE) OR TETRAHYDRO
FOLATE) (W) (DEHYDROGENASE OR DE HYDROGENASE) OR FOLIC(1W)RED
UCTASE
L15 52430 SEA FILE=HCAPLUS ABB=ON PLU=ON (PRODUCING OR PRODUCE# OR
PRODUCTION OR MANUF?) (S)ANTIBOD?
L16 257 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND (L5 OR L6 OR
GLUTAMINE SYNTHETASE)
L17 46 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND (LIGHT CHAIN OR
LC)
L18 38 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND (HEAVY CHAIN OR
HC)
L19 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 AND CELL
L20 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND (POLYPROTEIN OR
POLYPEPTIDE OR PEPTIDE OR PROTEIN)

L20 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 09 Nov 2005

ACCESSION NUMBER: 2005:1190118 HCAPLUS

TITLE: Bi-cistronic expression of anti-HBsAg based on Flp
recombination targeting and IRES sequence

AUTHOR(S): Ruan, Chengmai; Zhao, Jinhong; An, Xiaoping; Li,
Jianmin; Hao, Xiaomeng; Tong, Yigang; Chen, Wei;
Wang, Haitao

CORPORATE SOURCE: Institute of Microbiology and Epidemiology,
Academy of Military Medical Sciences, Beijing,
100071, Peop. Rep. China

SOURCE: Junshi Yixue Kexueyuan Yuankan (2004), 28(5),
427-429

CODEN: JYKYEL; ISSN: 1000-5501

PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The expression efficiency of whole antibodies that are different in
construction was compared. A bi-cistronic antibody expression vector
was constructed that included FLP recombination site and ECMV-IRES
sequence. The **light chain** was inserted
up-streamly to the IRES site, and in down-stream multi-cloning site,
the **heavy chain** was inserted. The construct was

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transfected into CHO/**dhfr** cell with LipofectAMINE.
In transient expression, no detectable **antibody** expression was **produced** in ELISA assay, but in stable clone selected with blamycin, the **antibody** was detected, and the expression variance was less than 40%. It was proved that the construct is a promising tool for **protein** expression level comparing.

L20 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 07 Oct 2005

ACCESSION NUMBER: 2005:1078101 HCAPLUS

DOCUMENT NUMBER: 143:365642

TITLE: Retroviral vectors comprising exogenous promoter and amplifiable marker for integrating into host **cell** chromosome to produce recombinant **protein** or immunoglobulin

INVENTOR(S): Bleck, Gregory T.

PATENT ASSIGNEE(S): Cardinal Health Pts, LLC, USA

SOURCE: U.S. Pat. Appl. Publ., 142 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005221429	A1	20051006	US 2005-36557	20050114
PRIORITY APPLN. INFO.:			US 2004-537462P	P 20040116

AB The present invention relates to the production of **proteins** in host **cells**, and more particularly to host **cells** containing multiple integrated copies of an integrating vector comprising an exogenous gene and an amplifiable marker. The amplifiable marker is selected from **DHFR** and **glutamine synthetase**. The exogenous gene or transgene comprises signal sequence, MoMLV element, IRES element, polycistronic sequence and/or gene encoding IgG, IgA, IgM, IgD, IgE or sIg. The host **cell** is selected from CHO **cell**, baby hamster kidney **cell**, human 293 **cell** and bovine mammary epithelial **cell**. The present invention further provides methods of expressing increased levels of recombinant **protein** in host **cells** using such vectors.

IT 9002-03-3, Dihydrofolate reductase

9023-70-5, Glutamine synthetase

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(retroviral vectors comprising exogenous promoter and amplifiable marker for integrating into host **cell** chromosome to produce recombinant **protein** or Ig)

L20 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 29 Jul 2005

ACCESSION NUMBER: 2005:672773 HCAPLUS

DOCUMENT NUMBER: 143:152011

TITLE: Overexpression of enzymes involved in post-translational **protein** modifications in human **cells**

INVENTOR(S): Uytdehaag, Alphonsus G. C. M.; Opstelten, Dirk J. E.

Searcher : Shears 571-272-2528

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PATENT ASSIGNEE(S): Neth.
 SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of
 U.S. Ser. No. 497,832.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 10
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 2005164386	A1	20050728	US 2004-26518	20041230
US 6855544	B1	20050215	US 2000-549463	20000414
WO 2003048348	A2	20030612	WO 2002-NL804	20021209
WO 2003048348	A3	20031211		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005181359	A1	20050818	US 2005-102073	20050408
PRIORITY APPLN. INFO.:			US 1999-129452P	P 19990415
			US 2000-549463	A2 20000414
			WO 2002-NL804	W 20021209
			US 2005-497832	A2 20050110
			WO 2001-NL792	A 20011029
			WO 2001-NL892	A 20011207
			EP 2002-75327	A 20020125
			WO 2002-NL257	A 20020419
			WO 2002-NL686	W 20021029
			US 2004-494140	A2 20040429
			US 2004-26518	A2 20041230

AB Methods and compns. for the production of recombinant **proteins** in a human **cell** line are provided. The methods and compns. are particularly useful for generating stable expression of human recombinant **proteins** of interest that are modified post-translationally, for example, by glycosylation. Such **proteins** may have advantageous properties in comparison with their counterparts produced in non-human systems such as Chinese hamster ovary **cells**. Immortalized human embryonic retina **cells** (PER.C6) comprising a nucleic acid sequence encoding an adenoviral E1A **protein** integrated into the genome of the

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cells and a nucleic acid sequence encoding an enzyme involved in post-translational modification of **proteins**, wherein said nucleic acid sequence encoding the enzyme involved in post-translational modification of **proteins** is under control of a heterologous promoter are further disclosed. Over-expression of ElB **protein** acts to inhibit apoptosis. Methods for production of recombinant **proteins** from such **cells** and obtaining such recombinant **proteins** having increased sialylation are provided by recombinant co-expression of α -2,6-sialyltransferase or α -2,3-sialyltransferase. Increase of sialic acid content in recombinantly produced erythropoietin results in an increased erythropoietic activity.

IT **9002-03-3P, Tetrahydrofolate Dehydrogenase**

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

(recombinant **protein** production in human **cell**

PER.C6 transformed with adenoviral El **protein** genes)

L20 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 27 May 2005

ACCESSION NUMBER: 2005:453802 HCAPLUS

DOCUMENT NUMBER: 142:476236

TITLE: **Protein A** or other lymphocyte differentiation factor for immunomodulation, compositions and methods of use

INVENTOR(S): Mann, Paul

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 121,481.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005113299	A1	20050526	US 2004-941636	20040915
US 2003211986	A1	20031113	US 2002-121481	20020410
WO 2003086317	A2	20031023	WO 2003-US7019	20030306
WO 2003086317	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-121481 A2 20020410

WO 2003-US7019 A2 20030306

AB Methods and compns. for modulating an immune response in a subject are provided. Methods include administering to the subject a composition comprising an effective amount of a lymphocyte differentiation factor,

Searcher : Shears 571-272-2528

10/719006

e.g., **protein A (PA)**, sufficient to modulate the immune response. Compns. include a lymphocyte differentiation factor, e.g., PA, in an amount less than 1 µg. PA administered at very low concns. reduced inflammation and inhibited or reversed tissue damage caused by the inflammation in arthritis animal models.

IT **9026-93-1, Adenosine deaminase**

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(deficiency, treatment of; **protein A** or other lymphocyte differentiation factor for immunomodulation)

L20 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 21 Jan 2005

ACCESSION NUMBER: 2005:58349 HCAPLUS

DOCUMENT NUMBER: 142:128717

TITLE: Episomal replication-competent transient expression vectors for eukaryotic hosts including a scaffold attachment region

INVENTOR(S): Ivanova, Lidia; Saudan, Philippe

PATENT ASSIGNEE(S): Cytos Biotechnology AG, Switz.

SOURCE: PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005644	A1	20050120	WO 2004-EP7556	20040709
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005064467	A1	20050324	US 2004-888961	20040712
PRIORITY APPLN. INFO.:			US 2003-486238P	P 20030711
			US 2003-524852P	P 20031126
			WO 2004-EP7556	A 20040709

AB Transient expression plasmid vectors for eukaryotic **cells** that can drive high levels of expression are described. These vectors may be used for the short term, high-level expression of a foreign gene, e.g. in the treatment of disease (no data.). The plasmids carry one or more replication origins and one or more genes for replication initiation factors. They also carry a scaffold/matrix attachment region (S/MAR), preferably derived from the interferon β gene. Inclusion of the matrix attachment region greatly increases the level of expression of genes borne by the vector. Expression is driven by a strong promoter and the expression cassette contains other elements

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that improve levels or stability of the transcript. Use of oriP and the EBNA1 gene of Epstein-Barr virus to make the plasmid replication competent is demonstrated.

IT **9023-70-5, Glutamine synthetase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for, as marker in expression vectors; episomal
replication-competent transient expression vectors for eukaryotic
hosts including scaffold attachment region)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L20 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 03 Dec 2004

ACCESSION NUMBER: 2004:1038669 HCAPLUS

DOCUMENT NUMBER: 142:22311

TITLE: Mouse/human chimeric anti-phencyclidine antibody
for treating arylcyclohexylamine drug abuse or
overdose

INVENTOR(S): Owens, S. Michael; Lacy, H. Marie

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 34 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004242848	A1	20041202	US 2004-828782	20040421
PRIORITY APPLN. INFO.:			US 2003-464190P	P 20030421

AB The present invention provides a chimeric mouse/human antibody (ch-mAb6B5) for treatment of abuse and toxicity of the arylcyclohexylamines class of drugs (i.e., phencyclidine- or PCP-like drugs). This antibody comprises light and **heavy chain** PCP binding regions of mouse mAb6B5, coupled to the light and **heavy chain** constant regions of a human kappa IgG2 or IgG4 isoform. Also provided are the DNA and amino acid sequences of the chimeric light and **heavy chain** of this antibody. Further provided are data that demonstrate that the new chimeric antibody retains the high affinity and specificity of a previously generated mouse anti-PCP monoclonal antibody (mAb6B5) yet being minimally immunogenic since it has human Ig constant region. This new medication would allow safe and effective treatment of PCP drug overdose, decrease mortality, and reduce harmful effects due to excessive and prolonged PCP drug use.

L20 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 26 Nov 2004

ACCESSION NUMBER: 2004:1019664 HCAPLUS

DOCUMENT NUMBER: 142:1781

TITLE: Production of host **cells** containing
multiple integrating retroviral vectors by serial
transduction

INVENTOR(S): Bleck, Gregory T.; Bremel, Robert D.; Miller,
Linda U.

PATENT ASSIGNEE(S): Gala Design, Inc., USA

Searcher : Shears 571-272-2528

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SOURCE: U.S. Pat. Appl. Publ., 143 pp., Cont.-in-part of
U.S. Ser. No. 397,079.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004235173	A1	20041125	US 2004-759315	20040116
US 2003092882	A1	20030515	US 2001-897511	20010629
US 6852510	B2	20050208		
US 2003224415	A1	20031204	US 2003-397079	20030326
US 2005100952	A1	20050512	US 2004-18895	20041221
WO 2005072129	A2	20050811	WO 2005-US1165	20050114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-215925P	P 20000703
			US 2001-897511	A2 20010629
			US 2003-397079	A2 20030326
			US 2002-368357P	P 20020328
			US 2004-759315	A 20040116

AB The present invention relates to the production of **proteins** in host **cells**, and more particularly to host **cells** containing multiple integrated copies of an integrating vector comprising an exogenous gene and methods of making such host **cells** by serial transduction or transfection. The present invention further provides methods of expressing increased levels of **protein** in host **cells** using such vectors.

IT 9002-03-3P, Dihydrofolate reductase

9023-70-5P, Glutamine synthetase

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(as amplifiable marker; production of host **cells** containing multiple integrating retroviral vectors by serial transduction)

L20 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 16 Nov 2004

ACCESSION NUMBER: 2004:977360 HCAPLUS

DOCUMENT NUMBER: 142:154330

TITLE: Comparative proteomic analysis of GS-NSO murine myeloma **cell** lines with varying recombinant monoclonal **antibody**

Searcher : Shears 571-272-2528

10/719006

production rate
AUTHOR(S): Smales, C. M.; Dinnis, D. M.; Stansfield, S. H.;
Alete, D.; Sage, E. A.; Birch, J. R.; Racher, A.
J.; Marshall, C. T.; James, D. C.
CORPORATE SOURCE: Research School of Biosciences, University of
Kent, Canterbury, CT2 7NJ, UK
SOURCE: Biotechnology and Bioengineering (2004), 88(4),
474-488
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have employed an inverse engineering strategy based on quant.
proteome anal. to identify changes in intracellular **protein**
abundance that correlate with increased specific recombinant
monoclonal **antibody production** (qMab) by engineered
murine myeloma (NSO) **cells**. Four homogeneous NSO
cell lines differing in qMab were isolated from a pool of
primary transfectants. The proteome of each stably transfected
cell line was analyzed at mid-exponential growth phase by
two-dimensional gel electrophoresis (2D-PAGE) and individual
protein spot volume data derived from digitized gel images were
compared statistically. To identify changes in **protein**
abundance associated with qMab datasets were screened for
proteins that exhibited either a linear correlation with
cell line qMab or a conserved change in abundance specific
only to the **cell** line with highest qMab. Several
proteins with altered abundance were identified by mass
spectrometry. **Proteins** exhibiting a significant increase in
abundance with increasing qMab included mol. chaperones known to
interact directly with nascent Igs during their folding and assembly
(e.g., BiP, endoplasmic, **protein** disulfide isomerase).
2D-PAGE anal. showed that in all **cell** lines Mab
light chain was more abundant than **heavy**
chain, indicating that this is a likely prerequisite for
efficient Mab production. In summary, these data reveal both the adaptive
responses and mol. mechanisms enabling mammalian **cells** in
culture to achieve high-level recombinant monoclonal **antibody**
production

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L20 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 16 Nov 2004

ACCESSION NUMBER: 2004:973454 HCAPLUS

DOCUMENT NUMBER: 142:92297

TITLE: On the Optimal Ratio of Heavy to **Light**
Chain Genes for Efficient Recombinant
Antibody Production by CHO
Cells

AUTHOR(S): Schlatter, Stefan; Stansfield, Scott H.; Dinnis,
Diane M.; Racher, Andrew J.; Birch, John R.;
James, David C.
CORPORATE SOURCE: School of Engineering, University of Queensland,
4072, Australia
SOURCE: Biotechnology Progress (2005), 21(1), 122-133
CODEN: BIPRET; ISSN: 8756-7938
PUBLISHER: American Chemical Society

Searcher : Shears 571-272-2528

10/719006

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monoclonal antibodies (Mab) are heterotetramers consisting of an equimolar ratio of **heavy chain (HC)** and **light chain (LC) polypeptides**. Accordingly, most recombinant Mab expression systems utilize an equimolar ratio of **heavy chain (hc)** to **light chain (lc)** genes encoded on either one or two plasmids. However, there is no evidence to suggest that this gene ratio is optimal for stable or transient production of recombinant Mab. In this study we have determined the optimal ratio of **hc:lc** genes for production of a recombinant IgG4 Mab, cB72.3, by Chinese hamster ovary (CHO) **cells** using both empirical and math. modeling approaches. Polyethyleneimine-mediated transient expression of cB72.3 at varying ratios of **hc:lc** genes encoded on sep. plasmids yielded an optimal Mab titer at a **hc:lc** gene ratio of 3:2; a conclusion confirmed by sep. math. modeling of the Mab folding and assembly process using transient expression data. On the basis of this information, we hypothesized that utilization of **hc** genes at low **hc:lc** gene ratios is more efficient. To confirm this, cB72.3 Mab was transiently produced by CHO **cells** at constant **hc** and varying **lc** gene dose. Under these conditions, Mab yield was increased with a concomitant increase in **lc** gene dose. To determine if the above findings also apply to stably transfected CHO **cells** producing recombinant Mab, we compared the intra- and extracellular ratios of **HC** and **LC polypeptides** for three **GS-CHO cells** lines transfected with a 1:1 ratio of **hc:lc** genes and selected for stable expression of the same recombinant Mab, cB72.3. Intra- and extracellular **HC:LC polypeptide** ratios ranged from 1:2 to 1:5, less than that observed on transient expression of the same Mab in parental CHO **cells** using the same vector. In conclusion, our data suggest that the optimal ratio of **hc:lc** genes used for transient and stable expression of Mab differ. In the case of the latter, we infer that optimal Mab production by stably transfected **cells** represents a compromise between **HC** abundance limiting productivity and the requirement for excess **LC** to render Mab folding and assembly more efficient.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 11 Nov 2004

ACCESSION NUMBER: 2004:958651 HCAPLUS

DOCUMENT NUMBER: 142:149757

TITLE: Bicistronic expression vector for animal **cells**, transformed **cell** line containing the same vector and method for **producing antibody proteins** using the same

INVENTOR(S): Jang, Hyeon Suk; Jung, Jong Geun; Park, U. Yeong; Ra, Geun Bae; Sim, Dong Seop; Yang, Jae Yeong; Yoo, Jin San; Yoon, Hye Seong

PATENT ASSIGNEE(S): Lg Life Sciences Ltd., S. Korea

SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7

Searcher : Shears 571-272-2528

10/719006

DOCUMENT TYPE: Patent
 LANGUAGE: Korean
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2003062118	A	20030723	KR 2002-2544	20020116
PRIORITY APPLN. INFO.:			KR 2002-2544	20020116

AB A bicistronic expression vector for animal **cells**, a transformed **cell** line containing the same vector and a method for **producing antibody proteins** using the same are provided, thereby effectively expressing various genes such as an antigen gene. A bicistronic expression vector for animal **cells** comprises a cytomegalovirus (CMV) promoter required for **producing** the transcriptional RNA, at least one foreign gene selected from **light chain** gene or **heavy chain** gene of an **antibody**, an IRES sequence, a selective gene and a poly(A) sequence, sequentially, wherein the selective gene is dihydroxyfolate reductase (**DHFR**) or neomycin resistance gene (NEOR); the bicistronic expression vector is selected from pLCM-MoK(KCTC 10151BP), pLCD-MoK(KCTC 10151BP), pLCN-MoH(KCTC 10150BP) and pANTIBODY(KCTC 10152BP). A transformed animal **cell** is produced by transformation with the bicistronic expression vector. A method for **producing** the foreign gene selected from the **light chain** or **heavy chain** of the **antibody** is characterized by culturing the transformed animal **cell**.

L20 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 27 Jun 2004

ACCESSION NUMBER: 2004:515705 HCAPLUS

DOCUMENT NUMBER: 141:66202

TITLE: Method for producing recombinant **protein** with high efficacy

INVENTOR(S): Saudan, Philippe; Hennecke, Frank; Bachmann, Martin F.; Stern, Dorothee M.

PATENT ASSIGNEE(S): Cytos Biotechnology Ag, Switz.

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004053137	A2	20040624	WO 2003-CH810	20031210
WO 2004053137	A3	20040812		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,			

Searcher : Shears 571-272-2528

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DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2002-432245P

P 20021211

AB The present invention relates to the field of gene expression technol. and the production of recombinant **polypeptides** and/or untranslated RNA mols. in host **cells**. In particular, the invention provides a method for the production of recombinant **polypeptides** and/or untranslated RNA mols. in host **cells** allowing the production of high amts. of those mols. in a very short time and with a high degree of reproducibility, in particular with respect to a, preferably, pre-defined standard and, thus, making the present invention particularly attractive for the production of **proteins** for clin. use and the production under Good Manufacturing Practice (GMP).

IT 9023-70-5, **Glutamine synthetase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as selection marker; method for producing recombinant
protein with high efficacy)

L20 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 18 Jun 2004

ACCESSION NUMBER: 2004:493884 HCAPLUS

DOCUMENT NUMBER: 141:48565

TITLE: Mutant neomycin phosphotransferase genes and
method for the selection of high-producing
recombinant **cells**

INVENTOR(S): Enenkel, Barbara; Sautter, Kerstin; Otto, Ralf;
Fieder, Juergen; Bergemann, Klaus

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.,
Germany

SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004050884	A2	20040617	WO 2003-EP13203	20031125
WO 2004050884	A3	20040715		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10330686	A1	20040617	DE 2003-10330686	20030708
CA 2507664	AA	20040617	CA 2003-2507664	20031125
EP 1567652	A2	20050831	EP 2003-812157	20031125
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,			

Searcher : Shears 571-272-2528

10/719006

PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003016525 A 20051004 BR 2003-16525 20031125
PRIORITY APPLN. INFO.: DE 2002-10256081 A 20021129

DE 2003-10330686 A 20030708

WO 2003-EP13203 W 20031125

AB The invention relates to novel modified neomycin phosphotransferase genes and the use thereof in a selection method for high-producing recombinant **cells**. The invention also relates to expression vectors containing a modified neomycin phosphotransferase gene and a gene of interest functionally fused to an heterologous promoter, and a method for producing heterologous gene products by using said expression vectors. Thus, numerous mutant neomycin phosphotransferase genes were created which encoded enzymes with decreased activity. CHO **cells** cotransformed with IgG2 **light chain** expression plasmid containing D227G neomycin phosphotransferase mutant gene as selectable marker and IgG2 **heavy chain** expression plasmid containing GFP and **DHFR** genes were selected with G418 and sorted by FACS then amplified using methotrexate. Pools with productivity of 20 pg IgG2 per **cell** per day were obtained.

IT **9002-03-3, Dihydrofolate reductase**

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(clone amplification using; mutant neomycin phosphotransferase genes and method for selection of high-producing recombinant **cells**)

L20 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 13 May 2004

ACCESSION NUMBER: 2004:390266 HCAPLUS

DOCUMENT NUMBER: 140:405477

TITLE: Chimeric and humanized mouse monoclonal anti-human IL-6 antibody CLB-8 and fragments for treatment of immune disease, infection and cancer

INVENTOR(S): Giles-Komar, Jill; Knight, David; Peritt, David; Trikha, Mohit

PATENT ASSIGNEE(S): Centocor, Inc., USA

SOURCE: PCT Int. Appl., 117 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039826	A1	20040513	WO 2002-US36213	20021026
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR,			

Searcher : Shears 571-272-2528

10/719006

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2467719 AA 20030513 CA 2002-2467719 20021026
BR 2002014168 A 20040914 BR 2002-14168 20021026
EP 1562968 A1 20050817 EP 2002-784436 20021026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
PT, IE, FI, CY, TR, BG, CZ, EE, SK
NO 2004002418 A 20040805 NO 2004-2418 20040610
PRIORITY APPLN. INFO.: US 2001-332437P P 20011114
US 2001-332743P P 20011114
WO 2002-US36213 W 20021026

AB The present invention relates to at least one novel chimeric, humanized or CDR-grafted anti-IL-6 antibodies derived from the murine CLB-8 antibody, including isolated nucleic acids that encode at least one such anti-IL-6 antibody, vectors, host **cells**, transgenic animals or plants, methods of making and using thereof, including therapeutic compns., methods and devices.

IT **9002-03-3, Dihydrofolate reductase**
9023-70-5, Glutamine synthetase

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene; chimeric and humanized mouse monoclonal anti-human IL-6 antibody CLB-8 and fragments for treatment of immune disease, infection and cancer)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 20 Feb 2004

ACCESSION NUMBER: 2004:141669 HCAPLUS

DOCUMENT NUMBER: 140:216171

TITLE: Anti-PSMA antibodies and PSMA multimers for diagnosis, prognosis and therapy of prostatic or non-prostatic cancers

INVENTOR(S): Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schulke, Norbert; Gardner, Jason; Ma, Dangshe

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 151 pp., Cont.-in-part of Appl. No. PCT/US02/33944.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004033229	A1	20040219	US 2003-395894	20030321
WO 2003034903	A2	20030501	WO 2002-US33944	20021023
WO 2003034903	A3	20031030		
WO 2003034903	B1	20040513		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

Searcher : Shears 571-272-2528

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NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004161776 A1 20040819 US 2003-695667 20031027
US 2005215472 A1 20050929 US 2004-976352 20041027
PRIORITY APPLN. INFO.: US 2001-335215P P 20011023

US 2002-362747P P 20020307
US 2002-412618P P 20020920
WO 2002-US33944 A2 20021023
US 2003-395894 A2 20030321
US 2003-695667 A2 20031027

AB The invention includes **antibodies** or antigen-binding fragments thereof which bind specifically to conformational epitopes on the extracellular domain of prostate specific membrane antigen (PSMA), compns. containing one or a combination of such **antibodies** or antigen-binding fragments thereof, hybridoma **cell** lines that **produce** the **antibodies**, and methods of using the **antibodies** or antigen-binding fragments thereof for cancer diagnosis and treatment. The invention also includes oligomeric forms of PSMA **proteins**, compns. comprising the multimers, and antibodies that selectively bind to the multimers.

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-PSMA antibodies and PSMA multimers for diagnosis, prognosis and therapy of prostatic or non-prostatic cancers)

L20 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 31 Oct 2003

ACCESSION NUMBER: 2003:855544 HCAPLUS

DOCUMENT NUMBER: 139:346767

TITLE: Increasing yields of **proteins**
manufactured by expression of the cloned gene
using **cells** carrying multiple copies of
stable plasmid carrying multiple expression
cassettes

INVENTOR(S): Horwitz, Arnold H.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 133 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003203447	A1	20031030	US 2003-404724	20030331
CA 2492008	AA	20040422	CA 2003-2492008	20030331
WO 2004033693	A1	20040422	WO 2003-US10154	20030331

Searcher : Shears 571-272-2528

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1492874 A1 20050105 EP 2003-808015 20030331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005528925 T2 20050929 JP 2004-543182 20030331
PRIORITY APPLN. INFO.: US 2002-368530P P 20020329
WO 2003-US10154 W 20030331

AB A method of increasing the yield of a foreign **protein** from a producer **cell** using multiple copies of a vector carrying several copies of an expression cassette is described. Plasmids carrying multiple expression cassettes are stabilized against loss by internal recombination by placing selectable markers between the expression cassettes. The method is particularly useful for the manufacture of Igs, especially Igs with light and **heavy chains** from different sources. Copy number may be increased by repeated transformation of the host **cell** carrying the same expression cassettes, but with different selectable markers. The expression cassettes using strong promoters appropriate for high level gene expression in the host **cell**. The development of CHO-derived **cell** lines producing high levels of bactericidal/permeability-increasing **proteins** using three rounds of transformation and selection is demonstrated.

IT 9026-93-1, Adenosine deaminase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (gene for, as selectable marker; increasing yields of **proteins** manufactured by expression of cloned gene by increasing copy nos. of plasmid carrying multiple expression cassettes)

L20 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 09 Sep 2003

ACCESSION NUMBER: 2003:703715 HCAPLUS

DOCUMENT NUMBER: 140:13549

TITLE: Expression of whole human anti-HAV antibody in CHO **cells**

AUTHOR(S): Yu, Changming; Xu, Jing; Tong, Yigang; Chen, Wei; Liu, Guoqi; Xu, Zhikai; Wang, Haitao

CORPORATE SOURCE: Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing, 100071, Peop. Rep. China

SOURCE: Junshi Yixue Kexueyuan Yuankan (2002), 26(3), 176-178, 181

CODEN: JYKYEL; ISSN: 1000-5501

PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The CHO expression system for the whole human anti-hepatitis A virus (anti-HAV) antibody was developed. The **light chain**

Searcher : Shears 571-272-2528

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(VL-CL) of anti-HAV and its signal sequence were linked, then cloned into a mammalian expression vector, pCI-nec. The **heavy chain** signal sequence, the variable region, the first constant region(VH-Cm) and Fc fragment sequence were ligated to form a full length **heavy chain** ORE, which was then cloned into another mammalian expression vector, pCdhfr1. CHO/**dhfr** **cells** were cotransfected with the light and **heavy chain** expression vectors, and **cell** clones expressing human anti-HAV antibodies were selected by G418 and methotrexate (MTX). The recombinant human antibodies were purified with **protein** L affinity chromatog. from the **cell** culture medium. ELISA revealed that anti-HAV antibodies were expressed in culture medium. In reducing SDS-PAGE, the recombinant IgG exhibited two bands of approx. 50000 and 25000, resp. Western-blot demonstrated that both the whole IgG without reductant and the **heavy chain** with reductant reacted with goat anti-human Fc antiserum. Whole human anti-HAY **antibody** was expressed in CHO **cells**, which provides the basis for genetically engineered **production** of **antibody** with complete function.

L20 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 22 Aug 2003

ACCESSION NUMBER: 2003:656883 HCAPLUS

DOCUMENT NUMBER: 139:196281

TITLE: Fusion **proteins** comprising humanized anti-G250 antigen antibody and tumor necrosis factor fragment for therapeutic use

INVENTOR(S): Renner, Christoph; Scott, Andrew

PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA

SOURCE: PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068924	A2	20030821	WO 2003-US4243	20030212
WO 2003068924	A3	20041229		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004053365	A1	20040318	US 2003-365123	20030212
EP 1507859	A2	20050223	EP 2003-711002	20030212
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-355838P	P 20020213
			WO 2003-US4243	W 20030212

Searcher : Shears 571-272-2528

AB Chimeric antibodies, as well as fusion **proteins** which comprise chimeric or humanized antibodies, are disclosed. The antibodies are humanized murine antibodies specifically bind to GM-CSF, CD30, and G250 antigen. The fusion **proteins** include biol. active portions of tumor necrosis factor, or full length tumor necrosis factor. Expression vectors adapted for **production** of the **antibodies**, as well as methods for **manufacturing** these, are also disclosed.

IT **9002-03-3, Dihydrofolate reductase**
 RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (preparation of chimeric **proteins** comprising humanized anti-GM-CSF antibody and tumor necrosis factor for therapeutic use)

L20 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 22 Aug 2003

ACCESSION NUMBER: 2003:656879 HCAPLUS

DOCUMENT NUMBER: 139:196280

TITLE: Preparation of chimeric **proteins** comprising humanized anti-GM-CSF antibody and tumor necrosis factor for therapeutic use

INVENTOR(S): Renner, Christoph; Scott, Andrew; Burgess, Antony

PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068920	A2	20030821	WO 2003-US4185	20030212
WO 2003068920	C2	20040603		
WO 2003068920	A3	20040701		
WO 2003068920	C1	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004053365	A1	20040318	US 2003-365123	20030212
EP 1530580	A2	20050518	EP 2003-713430	20030212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			US 2002-355838P	P 20020213
WO 2003-US4185				W 20030212

AB Chimeric antibodies, as well as fusion **proteins** which comprise chimeric antibodies, are disclosed. The antibodies specifically bind to GM-CSF, CD30, and G250 antigen. The fusion

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proteins include biol. active portions of tumor necrosis factor, or full length tumor necrosis factor. Expression vectors adapted for **production** of the **antibodies**, as well as methods for **manufacturing** these, are also disclosed.

L20 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 16 May 2003

ACCESSION NUMBER: 2003:376298 HCAPLUS

DOCUMENT NUMBER: 138:384248

TITLE: Recombinant **protein** production in human
cell PER.C6 transformed with adenoviral E1
protein genes

INVENTOR(S): Bout, Abraham; Hateboer, Guus; Verhulst, Karina
Cornelia; Uytdehaag, Alphonsus Gerardus; Schouten,
Govert Johan

PATENT ASSIGNEE(S): Neth.

SOURCE: U.S. Pat. Appl. Publ., 61 pp., Division of U. S.
Ser. No. 549,463.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 10

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2003092160	A1	20030515	US 2002-234007	20020903
US 6855544	B1	20050215	US 2000-549463	20000414
US 2005170463	A1	20050804	US 2005-70890	20050302
PRIORITY APPLN. INFO.:			US 1999-129452P	P 19990415
			US 2000-549463	A3 20000414
			US 2002-234007	A2 20020903

AB Methods and compns. for the production of recombinant **proteins** in a human **cell** line. The methods and compns. are particularly useful for generating stable expression of human recombinant **proteins** of interest that are modified post-translationally, for example, by glycosylation. Such **proteins** may have advantageous properties in comparison with their counterparts produced in non-human systems such as Chinese hamster ovary **cells**. Thus, human **cell** line PER.C6 was transfected with plasmids containing the gene encoding the adenoviral transcription factor E2A and a variety of genes for **proteins** of interest.

IT 9002-03-3P, Tetrahydrofolate Dehydrogenase

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP
(Preparation)

(recombinant **protein** production in human **cell**
PER.C6 transformed with adenoviral E1 **protein** genes)

L20 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 02 May 2003

ACCESSION NUMBER: 2003:334823 HCAPLUS

DOCUMENT NUMBER: 138:352761

TITLE: Anti-prostate specific membrane antigen (PSMA)
antibodies and fragments for cancer diagnosis and
therapy and antitumor screening

Searcher : Shears 571-272-2528

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INVENTOR(S): Maddon, Paul J.; Donovan, Gerald P.; Olson,
William C.; Schuelke, Norbert; Gardner, Jason; Ma,
Dangshe
PATENT ASSIGNEE(S): PSMA Development Company, L.L.C., USA
SOURCE: PCT Int. Appl., 238 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003034903	A2	20030501	WO 2002-US33944	20021023
WO 2003034903	A3	20031030		
WO 2003034903	B1	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2464239	AA	20030501	CA 2002-2464239	20021023
EP 1448588	A2	20040825	EP 2002-802198	20021023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005523683	T2	20050811	JP 2003-537481	20021023
US 2004033229	A1	20040219	US 2003-395894	20030321
US 2004161776	A1	20040819	US 2003-695667	20031027
US 2005215472	A1	20050929	US 2004-976352	20041027
PRIORITY APPLN. INFO.:			US 2001-335215P	P 20011023
			US 2002-362747P	P 20020307
			US 2002-412618P	P 20020920
			WO 2002-US33944	W 20021023
			US 2003-395894	A2 20030321
			US 2003-695667	A2 20031027

AB The invention includes **antibodies** or antigen-binding fragments thereof which bind specifically to conformational epitopes on the extracellular domain of PSMA, compns. containing one or a combination of such **antibodies** or **antibodies** or antigen-binding fragments thereof, hybridoma **cell** lines that **produce** the **antibodies**, and methods of using the **antibodies** or antigen-binding fragments thereof for cancer diagnosis and treatment. The invention also includes oligomeric forms of PSMA **proteins**, compns. comprising the multimers, and antibodies that selectively bind to the multimers.

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST

Searcher : Shears 571-272-2528

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(Analytical study); BIOL (Biological study); USES (Uses)
(anti-prostate specific membrane antigen (PSMA) antibodies and
fragments for cancer diagnosis and therapy and antitumor screening)

L20 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 19 Sep 2002

ACCESSION NUMBER: 2002:709689 HCAPLUS

DOCUMENT NUMBER: 137:211928

TITLE: Construction of eukaryotic expression system and
its uses for antibody cloning

INVENTOR(S): Yang, Zhihua; Ran, Yuliang

PATENT ASSIGNEE(S): Institute of Tumors, Tumor Hospital, Chinese
Academy of Medical Sciences, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 31
pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1328157	A	20011226	CN 2000-108065	20000609
PRIORITY APPLN. INFO.:			CN 2000-108065	20000609

AB The invention relates to construction of plasmid vector for expression of antibody in eukaryote. The vector contains selective marker gene (such as aminoglycoside phosphate transferase, thymidine kinase, hygromycin B phosphate transferase, xanthine-guanine phosphoribosyltransferase, or asparagine synthase) and extensible selective marker gene (such as dihydrofolic acid reductase (**dhfr**) or **glutamine synthase**). The vector also contains weak promotor (such as 72 bp fragment-deleted SV40) for driving the expression of the said marker genes. The vector also contains strong promotor (such as PhCMV-IE, PSV40-E, or PRSV-LTR) for driving the expression of antibody gene. The vector also contains enhancer sequence (such as 5'-non-translational region SP163 of mouse vascular endothelial growth factor). The vector further contains strong translation terminator (such as BGH polyA or SV40 polyA). The eukaryotic expression system is constructed by successively preparing general cloning vectors (such as pYR-GCVH and pYR-GCVL) of variable region of antibody, intermediate expression vectors (such as pYR-SV2-rdhfr and pYR-SV2-rneo) of antibody, and general eukaryotic expression vector (such as pYR-GSEVH, pYR-GSEVL, pYR-GCEVH, and pYR-GCEVL). The eukaryotic expression system is used to preparation and **production of antibodies** (such as chimeric **antibody**, modified **antibody**, humanized **antibody**, small mol. **antibody**, intracellular **antibody**, double-specific **antibody**, and other derivs.). The chimeric antibody of human VEGF and small mol. antibody of human carcino-embryonic antigen (CEA) were prepared by using the eukaryotic expression system in CHO-**dhfr**- cell.

IT **9023-70-5, Glutamine synthase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective marker gene **GS** in vector from; construction of
eukaryotic expression system and its uses for antibody cloning)

IT **9002-03-3, Dihydrofolic acid reductase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

Searcher : Shears 571-272-2528

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(selective marker gene **dhfr** in vector from; construction
of eukaryotic expression system and its uses for antibody cloning)

L20 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 May 2002
ACCESSION NUMBER: 2002:354214 HCAPLUS
DOCUMENT NUMBER: 136:324066
TITLE: Humanized antibody to surface antigen pre-S2 of
hepatitis B virus, and preparation process thereof
INVENTOR(S): Park, Seong Seop; Huh, Hyang Suk; Hong, Hyo Jeong
PATENT ASSIGNEE(S): Korea Green Cross Corporation, S. Korea; Korea
Institute of Science and Technology
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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KR 2000055980	A	20000915	KR 1999-4939	19990212
PRIORITY APPLN. INFO.:			KR 1999-4939	19990212

AB A humanized antibody to surface antigen pre-S2 of hepatitis B virus (HBV) is provided, which maintains similar antigen-binding abilities with existing humanized antibody, but diminishes immune-causing abilities than existing humanized antibody obviously, so which can be used to prevent HBV infection and to treat the chronic hepatitis B. A process for the preparation of humanized **antibody** to HBV surface antigen pre-S2 comprises of: preparing humanized heavy-chained genes; preparing humanized light-chained genes; preparing representing vector (pCMV-HS2(II)HC) **producing humanized heavy** **-chain**; preparing representing vector (pKC-**dhfr** **-HS2(II)) producing humanized light-chain** ; culturing COS7 **cells**, and washing with OPTI MEM I; mixing pCMV-HS2(II)HC, pKC-**dhfr**-HS2(II) and Lipofectamine, adding OPTI MEM I, and pouring the mixture over the COS7 **cells**, culturing, concentrating, and measuring the concentration of the humanized **antibody** in COS7 **cell**; investigating binding ability of humanized **antibody** to HBV surface antigen pre-S2; and investigating binding affinity to antigen of humanized **antibody**.

L20 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 06 Oct 2000
ACCESSION NUMBER: 2000:707321 HCAPLUS
DOCUMENT NUMBER: 133:280571
TITLE: Process for **producing monoclonal** **antibody**
INVENTOR(S): Kusunoki, Chihiro; Fukushima, Atsushi
PATENT ASSIGNEE(S): Japan Tobacco Inc., Japan; Abgenix, Inc.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Searcher : Shears 571-272-2528

10/719006

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058499	A1	20001005	WO 2000-JP2022	20000330
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368734	AA	20001005	CA 2000-2368734	20000330
CA 2368734	C	20001005		
JP 2000342279	A2	20001212	JP 2000-97874	20000330
EP 1167537	A1	20020102	EP 2000-912975	20000330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 754808	B2	20021128	AU 2000-34563	20000330
PRIORITY APPLN. INFO.:			JP 1999-87929	A 19990330
			WO 2000-JP2022	W 20000330

AB Recombinant hybridomas are constructed by transferring a gene encoding an amino acid sequence, which is identical with the amino acid sequence of the **heavy chain polypeptide** of a specific monoclonal **antibody**, into immortalized B cells (hybridomas) **producing** this monoclonal **antibody**, thereby obtaining the monoclonal **antibody** in a significantly elevated amount from the liquid culture medium of the cells. Thus, transgenic mouse-**produced** human monoclonal anti-human interleukin 8 **antibody** was prepared and recombinant hybridoma K2.2.1 **producing** the anti-IL8 **antibody** was generated by introducing cDNA encoding secretory anti-human IL8 Ig. **heavy chain polypeptide**

IT **9002-03-3, Dihydrofolate reductase**
 RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (gene; process for **producing monoclonal antibody**)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
 ED Entered STN: 06 Oct 2000
 ACCESSION NUMBER: 2000:707212 HCAPLUS
 DOCUMENT NUMBER: 133:280568
 TITLE: Neutrokin-alpha binding **proteins** and methods based thereon
 INVENTOR(S): Ruben, Steven M.; Ullrich, Stephen; Baker, Kevin
 PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA
 SOURCE: PCT Int. Appl., 398 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 19
 PATENT INFORMATION:

Searcher : Shears 571-272-2528

10/719006

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058362	A1	20001005	WO 2000-US7966	20000324
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1577391	A1	20050921	EP 2005-12261	19961025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AU 2001054180	A5	20020725	AU 2001-54180	20010703
AU 779750	B2	20050210		
US 2002187526	A1	20021212	US 2002-84971	20020301
JP 2004129667	A2	20040430	JP 2003-362615	20031022
PRIORITY APPLN. INFO.:				
			US 1999-126599P	P 19990326
			US 2000-188208P	P 20000310
			AU 1996-76745	A3 19961025
			EP 1996-939612	A3 19961025
			JP 1998-520411	A3 19961025
			US 2000-533822	A1 20000324

AB The present invention relates to Neutrokin- α binding **polypeptides** (NAR). In particular, isolated nucleic acid mols. are provided encoding human NAR **protein**. NAR **polypeptides** are also provided as are vectors, host **cells** and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of NAR activity. The NAR **polypeptides, antibodies, agonists and antagonists** are useful for increasing B **cell** proliferation or Ig. **production**, and for treating immunodeficiencies and autoimmune diseases.

IT **9026-93-1, Adenosine deaminase**

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(deficiency; neutrokin- α receptor/binding **proteins** and antibodies for treating immunodeficiency and autoimmune diseases)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 13 May 1998

ACCESSION NUMBER: 1998:273604 HCAPLUS

DOCUMENT NUMBER: 129:40190

TITLE: Comparison of the **production** of a human monoclonal **antibody** against HIV-1 by

Searcher : Shears 571-272-2528

10/719006

heterohybridoma **cells** and recombinant
CHO **cells**: A flow cytometric study
AUTHOR(S): Borth, Nicole; Strutzenberger, Karl; Donalies,
Ute; Kunert, Renate; Katinger, Hermann
CORPORATE SOURCE: Institute for Applied Microbiology, University of
Agriculture, Vienna, 1190, Austria
SOURCE: Cytotechnology (1996), 22(1-3), 129-138
CODEN: CYTOER; ISSN: 0920-9069
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **production** of human monoclonal **antibodies** for
therapeutic use is of increasing importance for treatment of viral
infections such as AIDS. As human x mouse heterohybridomas rarely
reach the growth rates and **cell** specific production rates of
mouse hybridomas, the transfection of standard **cell** lines, such
as CHO or BHK, is a promising alternative. This has the addnl.
advantage that the IgG subtype can be changed to suit the desired
application. However, the use of a **cell** line that has not
originally developed to **produce antibodies**, as
lymphocytes and myeloma **cells** have, might have unrecognized
drawbacks. This will be especially significant in the case of antibodies as
each mol. consists of 4 chains linked by disulfide bonds which require
specific intracellular factors to be properly folded and processed (**Heavy chain binding protein**,
Protein Disulfide Isomerase a.o.). In this study, 2
cell lines were therefore compared: a human x mouse
heterohybridoma **producing** IAM-2F5, a human IgG3
antibody specific for HIV-1 with neutralizing properties, and
a Chinese Hamster Ovary **cell** transfected with
dihydrofolate reductase and with the heavy and
light chain genes of IAM-2F5 modified to IgG1. From
each **cell** line 3 subclones were selected with low, medium,
and high sp. production rates. Batch cultures were performed and the
following cellular parameters analyzed by flow cytometry, 1) total RNA
content (translational activity), 2) total **protein** content,
3) **cell** cycle phase distribution, 4) concentration of light and
heavy chains, 5) concentration of helper **proteins**
such as BiP and PDI. The production rate of heterohybridoma **cells**
was best reflected in the intracellular concentration of kappa chain, while
the gamma chain concentration was comparable for all 3 subclones. In the

CHO **cells** the gamma chain expression and thus gene copy number
appeared to be the limiting factor. The GRP78/BiP concentration in CHO
remained unchanged in spite of a 5-fold higher concentration of gamma chain
in the high producing subclone. The PDI concentration in CHO **cells**
was much lower compared to the heterohybridoma **cells**,
irresp. of production rates.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L20 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 16 May 1997

ACCESSION NUMBER: 1997:311170 HCAPLUS

DOCUMENT NUMBER: 126:304915

TITLE: A soluble derivative of a mammalian Fc receptor
with pH-dependent binding of antibodies

INVENTOR(S): Gastinel, Louis N.; Bjorkman, Pamela J.

Searcher : Shears 571-272-2528

10/719006

PATENT ASSIGNEE(S): California Institute of Technology, USA
 SOURCE: U.S., 30 pp., Cont. of U. S. Ser. No. 819,413,
 abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5623053	A	19970422	US 1993-4492	19930114
PRIORITY APPLN. INFO.:			US 1992-819413	B1 19920110

AB A soluble Fc receptor derivative (pHsFcR) that shows pH-regulated binding of antibodies is described. The receptor binds antibody in the pH range 5.5-6.5 and releases it in the pH range 7.5-8.5. This analog can still bind the β 2-microglobulin **light chain** to form a fully functional receptor. In particular, the pH-sensitive Fc receptors of neonates are preferred. These derivs. have uses in e.g. the purification of **antibodies manufactured** on a large or small scale. The pHsFcR is a C-terminal truncation derivative lacking the transmembrane domain manufactured by expression of a cDNA for the receptor carrying in-frame stop codons. The pHsFcR is secreted into the growth medium upon expression of the cDNA in a suitable (prokaryotic or eukaryotic) host and can be purified from the medium by affinity chromatog. against an immobilized antibody. A truncation derivs. of the rat intestinal neonatal Fc receptor were prepared using sequence similarities with class I MHC antigens. Expression constructs for analogs carrying the phosphatidyl anchoring signal of decay-accelerating factor were constructed by standard methods. Bicistronic constructs carrying the gene for the β 2-microglobulin **light chain** were also constructed. Manufacture of these analogs in CHO **cells** is demonstrated.

L20 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
 ED Entered STN: 14 May 1994
 ACCESSION NUMBER: 1994:242521 HCAPLUS
 DOCUMENT NUMBER: 120:242521
 TITLE: Monoclonal and humanized antibodies to P-selectin
 and their therapeutic uses
 INVENTOR(S): Chestnut, Robert W.; Polley, Margaret J.; Paulson,
 James C.
 PATENT ASSIGNEE(S): Cytel Corp., USA
 SOURCE: PCT Int. Appl., 80 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321956	A1	19931111	WO 1993-US4274	19930504
W:	AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			

Searcher : Shears 571-272-2528

10/719006

EP 642356 A1 19950315 EP 1993-911098 19930504
EP 642356 B1 20030416
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, LU, MC, NL, SE
JP 08503360 T2 19960416 JP 1993-519623 19930504
JP 3720352 B2 20051124
NZ 286804 A 20000825 NZ 1993-286804 19930504
AT 237353 E 20030515 AT 1993-911098 19930504
ES 2197150 T3 20040101 ES 1993-911098 19930504
CA 2135083 C 20040106 CA 1993-2135083 19930504
US 5800815 A 19980901 US 1994-202047 19940225
WO 9425067 A1 19941110 WO 1994-US4935 19940504
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,
HU, JP, KG, KP, KR, KZ, LK, LU, LV
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE, BF, BJ, CF, CG, CI, CM, GA, GN
PRIORITY APPLN. INFO.: US 1992-880196 A2 19920505
NZ 1993-252542 A1 19930504
WO 1993-US4274 W 19930504
IL 1993-105614 A 19930505
US 1993-57292 B2 19930505
US 1994-202047 A 19940225

AB The present invention relates to compns. and methods for treating inflammation and other pathol. conditions using novel blocking P-selectin antibodies which inhibit binding of an antibody secreted by a **cell** line designated ATCC Accession Number HB11041 to P-selectin as measured by a competitive inhibition assay. The antibodies of the invention may be used in the treatment of e.g. inflammatory and thrombotic diseases. **Production** of blocking and nonblocking monoclonal **antibodies** and humanized **antibodies** is described. The antibodies of the invention were tested in e.g. treatment of acute lung injury, myocardial ischemia and reperfusion, and leukocyte-endothelial **cell** interactions induced by degranulation of tissue mast **cells**.

L20 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 07 Aug 1993

ACCESSION NUMBER: 1993:447362 HCAPLUS

DOCUMENT NUMBER: 119:47362

TITLE: Disease-associated human autoantibodies specific for human thyroid peroxidase

INVENTOR(S): Rapoport, Basil

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 211 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9305072	A1	19930318	WO 1992-US7381	19920828
W: AU, CA, FI, JP, KR, NO, US				

Searcher : Shears 571-272-2528

10/719006

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE
WO 9303146 A1 19930218 WO 1992-US6283 19920730
W: AU, CA, FI, JP, KR, NO, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
AU 9225557 A1 19930405 AU 1992-25557 19920828
JP 07506960 T2 19950803 JP 1992-505362 19920828
EP 668918 A1 19950830 EP 1992-919338 19920828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE
FI 9400732 A 19940428 FI 1994-732 19940216
NO 9400668 A 19940429 NO 1994-668 19940225
PRIORITY APPLN. INFO.: US 1991-750579 A2 19910828

WO 1992-US6283 A 19920730

US 1991-738040 A2 19910730

WO 1992-US7381 A 19920828

AB Disease-associated human autoantibodies specific for human thyroid peroxidase (hTPO) are disclosed. Organ-specific anti-TPO human autoantibodies are disclosed which have been cloned, allowing definition of the autoantibody repertoire and the autoantigenic domains, encompassing a restricted immunodominant region on TPO recognized by patients with autoimmune thyroid disease. Compns. and diagnostic and therapeutic applications are also disclosed. Recombinant **production** of a secretable, truncated TPO is described, as are overprodn. of hTPO in nonthyroid eukaryotic **cells**, mol. determination of a B-cell epitope of TPO, determination of the role of TPO carbohydrate moieties in **antibody** recognition in Hashimoto's thyroiditis, cloning of genes for organ-specific anti-TPO human autoantibodies, etc.

IT **9002-03-3, Dihydrofolate reductase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(plasmid with genes for human thyroid peroxidase and, enhancement
for production of human thyroid peroxidase in relation to)

FILE 'MEDLINE' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'BIOSIS' ENTERED AT 17:01:20 ON 11 JAN 2006
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FILE 'JICST-EPLUS' ENTERED AT 17:01:20 ON 11 JAN 2006
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FILE 'JAPIO' ENTERED AT 17:01:20 ON 11 JAN 2006
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Searcher : Shears 571-272-2528

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L21 30 S L20
L22 24 DUP REM L21 (6 DUPLICATES REMOVED)

L22 ANSWER 1 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-372382 [38] WPIDS
DOC. NO. CPI: C2005-115433
TITLE: New plasmid system comprises a first universal transfer vector, a second universal transfer vector, and an amplifiable vector, useful for expressing multi-subunit complex **proteins** including antibodies and receptors.
DERWENT CLASS: B04 D16
INVENTOR(S): SAHA, D P
PATENT ASSIGNEE(S): (SCHE) SCHERING CORP
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005047512	A2	20050526	(200538)*	EN	164
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2005176099	A1	20050811	(200553)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005047512	A2	WO 2004-US37721	20041110
US 2005176099	A1 Provisional	US 2003-519230P	20031112
		US 2004-986498	20041110

PRIORITY APPLN. INFO: US 2003-519230P 20031112; US
2004-986498 20041110

AN 2005-372382 [38] WPIDS

AB WO2005047512 A UPAB: 20050616

NOVELTY - A plasmid system (I) comprising in separate containers, a first universal transfer vector, a second universal transfer vector, and an amplifiable vector, is new.

DETAILED DESCRIPTION - A plasmid system comprising in separate containers:

(a) a first universal transfer vector comprising a first multiple cloning site and a nucleotide sequence comprising fully defined 2935 base pair (bp) sequence (SEQ ID NO. 2) given in the specification, where the first multiple cloning site is Bss HII, Pme I, Sna BI, Hin dIII, Asp 718, Kpn I, Pae R71, Xho I, Sal I, Acc I, Hinc II, Cla I, Eco RV, Eco RI, Pst I, Eco O1091, Apa I, Xma I, Bsp EI, Bam HI, Dsa I, Eag I, Ecl XI, Not I, Sac II, Xma III, Xba I, Sac I, Mlu I, Bcl I, Bsr GI, or Bss HII;

(b) a second universal transfer vector comprising a second multiple cloning site and a nucleotide sequence comprising fully defined 2941 bp sequence (SEQ ID NO. 1) given in the specification,

Searcher : Shears 571-272-2528

where the second multiple cloning site is Bss HII, Sgr AI, Xma I, Rsr II, Spe I, Sna BI, Hin dIII, Asp 718, Kpn I, Pae R71, Xho I, Sal I, Acc I, Hinc II, Cia I, Eco RV, Eco RI, Pst I, Eco O1091, Apa I, Xma I, Bsp EI, Bam HI, Dsa I, Eag I, Ecl XI, Not I, Sac II, Xma III, Xba I, Sac I, Nde I, Msc II, Nru I, Pac I, or Bss HII; and

(c) an amplifiable vector comprising a third multiple cloning site and a nucleotide sequence comprising fully defined 5144 bp sequence (SEQ ID NO. 3) given in the specification, where the third multiple cloning site is Sgr AI, Srf I, Xma I, Spe I, Sac II, Rsr II, Pac I, Nru I, Not I, Nde I, Msc I, Mlu I, Kpn I, Fse I, Bss HII, Bsr GI, Bsp EI, Bcl I, Bbv CI, Pme I, Bss HII, Asc I, or Xba I.

INDEPENDENT CLAIMS are also included for:

(1) producing a **protein** (M1) comprising two or more types of **polypeptide**;

(2) **producing** an anti-IGFR1 **antibody** (M2);

(3) a kit comprising the plasmid system and one or more components selected from sterile, distilled water; calcium phosphate transformation reagents CaCl₂ and 2X HEPES buffered saline; DEAE-dextran transformation reagents chloroquine in Phosphate buffered saline and phosphate buffered saline; DOTAP/cholesterol extruded liposomes; Transformation competent *Escherichia coli*; Dulbecco/Vogt modified Eagle's minimal essential medium (DMEM); Fetal calf serum; luria broth media; or paper instructions for usage of the plasmid system;

(4) an oligonucleotide primer comprising a nucleotide sequence selected from 3 fully defined 155, 160, or 166 base pair (bp) sequences (SEQ ID NO. 10, 11, or 12) given in the specification; and

(5) a plasmid comprising a nucleotide sequence selected from 4 fully defined 11520-13079 bp sequences (SEQ ID NO. 6-9) given in the specification.

USE - The plasmid system is useful for expressing multi-subunit complex **proteins** including antibodies and receptors (claimed). The plasmid system is used for recombinant **protein** expression in any **cell**, including mammalian **cell**, bacterial **cell**, yeast **cell**, or insect **cell**

Dwg.0/16

L22 ANSWER 2 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2005-322962 [33] WPIDS
 DOC. NO. CPI: C2005-100779
 TITLE: New chromatin insulator, useful in expressing a gene of interest, in simultaneously expressing two or more genes or DNAs of interest or in the manufacture of a medicament for DNA-based therapy.
 DERWENT CLASS: B04 D16
 INVENTOR(S): CHATELLARD, P; IMHOF, M
 PATENT ASSIGNEE(S): (ISTF) ARS APPLIED RES SYSTEMS HOLDING NV
 COUNTRY COUNT: 108
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005040384	A1	20050506	(200533)*	EN	30
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT					
KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG					
ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ					
DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP					

10/719006

KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA
NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR
TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005040384	A1	WO 2004-EP52591	20041020

PRIORITY APPLN. INFO: EP 2003-103890 20031021

AN 2005-322962 [33] WPIDS

AB WO2005040384 A UPAB: 20050524

NOVELTY - A new chromatin insulator comprising a sequence having 146 bp (SEQ ID Number 1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a vector comprising one or more insulators;

(2) a host **cell** comprising the insulator or transfected with the vector; and

(3) producing a **polypeptide** of interest.

ACTIVITY - None given.

MECHANISM OF ACTION - Gene Therapy.

USE - The vector is useful in expressing a gene of interest, in simultaneous expression of two or more genes or DNAs of interest or in the manufacture of a medicament for DNA-based therapy (claimed).

Dwg.0/5

L22 ANSWER 3 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-092088 [10] WPIDS

DOC. NO. CPI: C2005-031170

TITLE: New nucleic acid molecule having a gene of interest, a scaffold/matrix attached region one an origin of replication, and a replication initiation factor, useful for expressing recombinant **proteins**.

DERWENT CLASS: B04 D16

INVENTOR(S): IVANOVA, L; SAUDAN, P

PATENT ASSIGNEE(S): (CYTO-N) CYTOS BIOTECHNOLOGY AG

COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005005644	A1	20050120	(200510)*	EN	105
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2005064467	A1	20050324	(200526)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005005644	A1	WO 2004-EP7556	20040709

Searcher : Shears 571-272-2528

10/719006

US 2005064467	A1 Provisional	US 2003-486238P	20030711
	Provisional	US 2003-524852P	20031126
		US 2004-888961	20040712

PRIORITY APPLN. INFO: US 2003-524852P 20031126; US
2003-486238P 20030711

AN 2005-092088 [10] WPIDS

AB WO2005005644 A UPAB: 20050211

NOVELTY - A nucleic acid molecule comprising at least one gene of interest, at least one scaffold/matrix attached region (S/MAR), at least one origin of replication (ORI), and at least one replication initiation factor capable of recognizing the at least one origin of replication, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an expression system comprising at least one nucleic acid molecule cited above, or at least one gene of interest, at least one S/MAR, at least one ORI, and at least one replication initiation factor capable of recognizing the at least one origin of replication;

(2) preparation of the nucleic acid molecule cited above, comprising inserting at least one S/MAR into a nucleic acid construct having at least one ORI, at least one gene of interest and at least one replication initiation factor;

(3) making a recombinant host **cell**, comprising introducing the nucleic acid molecule cited above or the expressions system of (1) into a host **cell**;

(4) a recombinant host **cell** produced by the method of (3), and comprising the nucleic acid molecule cited above, and/or at least one gene of interest, at least one S/MAR, at least one ORI, and at least one replication initiation factor capable of recognizing the at least one origin of replication;

(5) producing a **polypeptide** or untranslated RNA molecule, comprising introducing the nucleic acid molecule cited above or expression system of (1) into a host **cell** to produce a recombinant host **cell**, and culturing the **cell** for expression of the **polypeptide** or untranslated RNA molecule;

(6) a kit comprising the nucleic acid molecule cited above or the recombinant host **cell** of (4), or a transfection system selected from a lipid, polymer, **peptide** or porphyrin; and

(7) a kit for the production of a **polypeptide** or untranslated RNA molecule, comprising at least one nucleic acid molecule cited above or at least one recombinant host **cell** of (4).

MECHANISM OF ACTION - Vaccine.

No biological data given.

USE - The methods and compositions of the present invention are useful for the high level expression of **polypeptides** and/or untranslated RNA molecules, in particular for the rapid **production** of large quantities of recombinant **proteins** such as monoclonal **antibodies**, which can be used as drugs.
Dwg.0/3

L22 ANSWER 4 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-394969 [40] WPIDS

CROSS REFERENCE: 2003-845257 [78]

DOC. NO. CPI: C2005-122131

TITLE: Modulating an immune response for treating an immune dysfunction in a subject by administering a composition comprising a lymphocyte differentiation

Searcher : Shears 571-272-2528

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factor.
DERWENT CLASS: B04
INVENTOR(S): MANN, P
PATENT ASSIGNEE(S): (MANN-I) MANN P
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2005113299	A1	20050526	(200540)*		27

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005113299	A1 CIP of	US 2002-121481	20020410
	CIP of	WO 2003-US7019	20030306
		US 2004-941636	20040915

PRIORITY APPLN. INFO: US 2004-941636 20040915; US
2002-121481 20020410; WO
2003-US7019 20030306

AN 2005-394969 [40] WPIDS

CR 2003-845257 [78]

AB US2005113299 A UPAB: 20050624

NOVELTY - Modulating an immune response in a subject comprising administering to the subject a composition containing a lymphocyte differentiation factor sufficient to modulate the immune response, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) treating an immune dysfunction in a subject with or at risk of an immune dysfunction;

(2) reducing an inflammatory response in a subject with or at risk of an inflammatory response;

(3) treating inflammation in a subject with or at risk of inflammation;

(4) inhibiting tissue or **cell** damage in a subject caused by an inflammatory response or inflammation;

(5) treating existing tissue or **cell** damage in a subject caused by an inflammatory response or inflammation;

(6) treating splenomegaly in a subject;

(7) inhibiting proliferation or survival of a splenocyte in a subject having or at risk of having undesirable splenocyte proliferation or survival;

(8) stimulating differentiation or apoptosis of a splenocyte in a subject having or at risk of having undesirable splenocyte proliferation or apoptosis;

(9) reducing **antibody production** by a splenocyte in a subject having or at risk of having undesirable numbers of an **antibody**;

(10) reducing natural killer (NK) **cell** cytotoxicity in a subject having or at risk of having undesirable NK **cell** cytotoxicity;

(11) inhibiting rejection of a transplanted **cell**, tissue or organ in a subject;

(12) stimulating differentiation of lymphoid **cells**;

(13) a pharmaceutical composition comprising a unit dosage form

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of PA sufficient to reduce an inflammatory response, inflammation in a subject; and

(14) a kit comprising a unit dosage form of PA to reduce an inflammatory response, inflammation or tissue or **cell** damage caused by an inflammatory response or inflammation in a subject, and instructions for use.

ACTIVITY - Antiinflammatory; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The method is useful in modulating an immune response for treating an immune dysfunction in a subject. The immune dysfunction comprises an autoimmune disorder. The autoimmune disorder comprises severe combined immunodeficiency (SCID), recombinae activating gene (RAG 1/2) deficiency, **adenosine deaminase** (ADA) deficiency, interleukin receptor chain deficiency, Janus-associated kinase 3 (JAK3) deficiency, reticular dysgenesis, primary T **cell** immunodeficiency, DiGeorge syndrome, Nude syndrome, T **cell** receptor deficiency, major histocompatibility complex (MHC) class II deficiency, TAP-2 deficiency (MHC class I deficiency), ZAP70 tyrosine kinase deficiency, purine nucleotide phosphorylase (PNP) deficiency, an **antibody** deficiency, X-linked agammaglobulinemia (Bruton's tyrosine kinase deficiency), autosomal recessive agammaglobulinemia, Mu **heavy chain** deficiency, surrogate **light chain** (5/14.1) deficiency, Hyper-IgM syndrome, X-linked (CD40 ligand deficiency), Ig **heavy chain** gene deletion, IgA deficiency, deficiency of IgG subclasses with and without IgA deficiency, common variable immunodeficiency (CVID), **antibody** deficiency with normal immunoglobulins, transient hypogammaglobulinemia of infancy, interferon receptor (IFNGR1 or IFNGR2) deficiency, interleukin 12 deficiency, interleukin 12 receptor deficiency, immunodeficiency with thymoma, Wiskott-Aldrich syndrome (WAS **protein** deficiency), ataxia telangiectasia (ATM deficiency), X-linked lymphoproliferative syndrome (SH2D1A/SAP deficiency) and hyper IgE syndrome. The inflammation is chronic or acute. The inflammation is at least in part **antibody** or **cell** mediated. The treatment results in a reduction in severity of a symptom of inflammation. The symptom comprises swelling, pain, headache, fever, nausea, skeletal joint stiffness, or tissue or **cell** damage. The treatment results in inhibition of **antibody production** or lymphoid **cell** proliferation. The tissue or **cell** damage is caused by a chronic or acute inflammatory response or inflammation. The inflammatory response or inflammation is at least in part **antibody** or **cell** mediated. The tissue or **cell** damage is present in thymus, liver, kidney, spleen, skin, or a skeletal joint. The skeletal joint comprises a knee, ankle, hip, shoulder, wrist, finger, toe or elbow. (All claimed.)
Dwg.0/1

L22	ANSWER 5 OF 24	MEDLINE on STN	DUPLICATE 1
ACCESSION NUMBER:	2005262531	MEDLINE	
DOCUMENT NUMBER:	PubMed ID: 15903249		
TITLE:	On the optimal ratio of heavy to light chain genes for efficient recombinant antibody production by CHO cells .		
AUTHOR:	Schlatter Stefan; Stansfield Scott H; Dinnis Diane M; Racher Andrew J; Birch John R; James David C		
CORPORATE SOURCE:	School of Engineering, University of Queensland, QLD		

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4072, Australia, and Lonza Biologics plc, 228 Bath Road, Slough SL1 4DX, UK.
SOURCE: Biotechnology progress, (2005 Jan-Feb) 21 (1) 122-33.
Journal code: 8506292. ISSN: 8756-7938.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 20050521
Last Updated on STN: 20050708
Entered Medline: 20050707

AB Monoclonal antibodies (Mab) are heterotetramers consisting of an equimolar ratio of **heavy chain (HC)** and **light chain (LC) polypeptides**. Accordingly, most recombinant Mab expression systems utilize an equimolar ratio of **heavy chain (hc)** to **light chain (lc)** genes encoded on either one or two plasmids. However, there is no evidence to suggest that this gene ratio is optimal for stable or transient production of recombinant Mab. In this study we have determined the optimal ratio of **hc:lc** genes for production of a recombinant IgG4 Mab, cB72.3, by Chinese hamster ovary (CHO) **cells** using both empirical and mathematical modeling approaches. Polyethyleneimine-mediated transient expression of cB72.3 at varying ratios of **hc:lc** genes encoded on separate plasmids yielded an optimal Mab titer at a **hc:lc** gene ratio of 3:2; a conclusion confirmed by separate mathematical modeling of the Mab folding and assembly process using transient expression data. On the basis of this information, we hypothesized that utilization of **hc** genes at low **hc:lc** gene ratios is more efficient. To confirm this, cB72.3 Mab was transiently produced by CHO **cells** at constant **hc** and varying **lc** gene dose. Under these conditions, Mab yield was increased with a concomitant increase in **lc** gene dose. To determine if the above findings also apply to stably transfected CHO **cells** producing recombinant Mab, we compared the intra- and extracellular ratios of **HC** and **LC polypeptides** for three GS-CHO **cells** lines transfected with a 1:1 ratio of **hc:lc** genes and selected for stable expression of the same recombinant Mab, cB72.3. Intra- and extracellular **HC:LC polypeptide** ratios ranged from 1:2 to 1:5, less than that observed on transient expression of the same Mab in parental CHO **cells** using the same vector. In conclusion, our data suggest that the optimal ratio of **hc:lc** genes used for transient and stable expression of Mab differ. In the case of the latter, we infer that optimal Mab production by stably transfected **cells** represents a compromise between **HC** abundance limiting productivity and the requirement for excess **LC** to render Mab folding and assembly more efficient.

L22 ANSWER 6 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-758278 [74] WPIDS
DOC. NO. CPI: C2004-266126
TITLE: New immunogenic recombinant antibody comprising a part of a murine IgG2a subtype amino acid sequence and a mammalian glycosylation, useful in preparing a vaccine for immunizing primates against infectious or

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autoimmune disorders.
DERWENT CLASS: B04 D16
INVENTOR(S): HIMMLER, G; LOIBNER, H; PUTZ, T; SCHUSTER, M;
WAXENECKER, G
PATENT ASSIGNEE(S): (IGEN-N) IGENEON KREBS IMMUNOTHERAPIE FORSCHUNGS
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004091655	A2	20041028	(200474)*	EN	59
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004091655	A2	WO 2004-EP4059	20040416

PRIORITY APPLN. INFO: AT 2003-599 20030417

AN 2004-758278 [74] WPIDS

AB WO2004091655 A UPAB: 20041117

NOVELTY - A new immunogenic recombinant antibody designed for immunization of primates comprises at least a part of a murine IgG2a subtype amino acid sequence and a mammalian glycosylation.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine comprising the antibody in a pharmaceutical formulation;

(2) a multicistronic **antibody** expression construct for **producing an antibody** in a Chinese Hamster Ovary (CHO) or HEK293 expression system, which contains at least a nucleotide sequence encoding a kappa **light chain** and a nucleotide sequence encoding a gamma **heavy chain**, where at least one of the nucleotide sequences encoding a kappa **light chain** or gamma **heavy chain** comprises a nucleotide sequence encoding at least a part of a murine IgG2a subtype amino acid sequence, and at least two IRES elements;

(3) a vector comprising a promoter, the antibody-expression construct and a transcription termination sequence;

(4) a CHO host **cell** or a HEK 293 transformed with the vector; and

(5) a method of **producing an antibody**.

ACTIVITY - Antimicrobial; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The immunogenic recombinant antibody is useful in preparing a vaccine for immunizing primates against infectious or autoimmune disorders.

Dwg.0/10

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L22 ANSWER 7 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-468875 [44] WPIDS
DOC. NO. CPI: C2004-175775
TITLE: Producing a **polypeptide** or untranslated RNA
molecule comprises introducing at least one nucleic
acid molecule into the at least one host **cell**
to produce at least one recombinant host **cell**
.
DERWENT CLASS: B04 D16
INVENTOR(S): BACHMANN, M F; HENNECKE, F; SAUDAN, P; STERN, D M
PATENT ASSIGNEE(S): (CYTO-N) CYTOS BIOTECHNOLOGY AG
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG																
WO 2004053137	A2	20040624	(200444)*	EN	63																
RW:	AT	BE	BG	BW	CH	CY	CZ	DE	DK	EA	EE	ES	FI	FR	GB	GH	GM	GR	HU	IE	IT
	KE	LS	LU	MC	MW	MZ	NL	OA	PT	RO	SD	SE	SI	SK	SL	SZ	TR	TZ	UG	ZM	ZW
W:	AE	AG	AL	AM	AT	AU	AZ	BA	BB	BG	BR	BY	BZ	CA	CH	CN	CO	CR	CU	CZ	DE
	DK	DM	DZ	EC	EE	ES	FI	GB	GD	GE	GH	GM	HR	HU	ID	IL	IN	IS	JP	KE	KG
	KP	KR	KZ	LC	LK	LR	LS	LT	LU	LV	MA	MD	MG	MK	MN	MW	MX	MZ	NI	NO	NZ
	OM	PG	PH	PL	PT	RO	RU	SC	SD	SE	SG	SK	SL	SY	TJ	TM	TN	TR	TT	TZ	UA
	UG	US	UZ	VC	VN	YU	ZA	ZM	ZW												
AU 2003283174	A1	20040630	(200472)																		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004053137	A2	WO 2003-CH810	20031210
AU 2003283174	A1	AU 2003-283174	20031210

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003283174	A1 Based on	WO 2004053137

PRIORITY APPLN. INFO: US 2002-432245P 20021211

AN 2004-468875 [44] WPIDS

AB WO2004053137 A UPAB: 20040712

NOVELTY - Producing a **polypeptide** or untranslated RNA
molecule comprising introducing at least one nucleic acid molecule
into the at least one host **cell** to produce at least one
recombinant host **cell**, is new.

DETAILED DESCRIPTION - Producing a **polypeptide** or
untranslated RNA molecule comprises:

(a) providing at least one host **cell**;

(b) introducing at least one nucleic acid molecule into the at
least one host **cell** to produce at least one recombinant host
cell, where the nucleic acid molecule comprises a first
polynucleotide element capable of replicating the at least one nucleic
acid molecule in said at least one host **cell**, and at least
one second polynucleotide element selected from an open reading frame
encoding a **polypeptide** of interest; a nucleotide sequence
complementary to all or a part of the open reading frame of (i); and a
nucleotide sequence encoding an untranslated RNA molecule or its

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complement;

(c) selecting at least one stable recombinant host cell from the at least one host cell;

(d) culturing the at least one recombinant host cell under conditions suitable for expression of the polypeptide or untranslated RNA molecule; and

(e) controlling the reproducibility of the method for producing the polypeptide or the untranslated RNA molecule as a function of time.

An INDEPENDENT CLAIM is included for a method for producing a polypeptide or untranslated RNA molecule conforming to Good Manufacturing Practice (GMP), comprising carrying out the steps of the novel method.

USE - The methods are useful for producing a polypeptide or untranslated RNA molecule (claimed).
Dwg.0/5

L22 ANSWER 8 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-419571 [39] WPIDS
DOC. NO. NON-CPI: N2004-333037
DOC. NO. CPI: C2004-157503
TITLE: New chimeric, humanized or CDR grafted antibody or its fragment capable of inhibiting human IL-6, useful for treating immune disorders, e.g. arthritis, inflammations, osteoporosis.
DERWENT CLASS: B04 D16 P13 P14
INVENTOR(S): GILES-KOMAR, J; KNIGHT, D; PERITT, D; TRIKHA, M; KNIGHT, D M; KOMAR, J G; MOHIT, T
PATENT ASSIGNEE(S): (CENZ) CENTOCOR INC
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004039826	A1	20040513	(200439)*	EN	117
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW					
BR 2002014168	A	20040914	(200469)		
AU 2002346369	A1	20040525	(200470)		
NO 2004002418	A	20040805	(200515)		
EP 1562968	A1	20050817	(200555)	EN	
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR					
TW 2003001134	A	20030701	(200556)#		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004039826	A1	WO 2002-US36213	20021026
BR 2002014168	A	BR 2002-14168	20021026
		WO 2002-US36213	20021026
AU 2002346369	A1	AU 2002-346369	20021026
NO 2004002418	A	WO 2002-US36213	20021026

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EP 1562968	A1	NO 2004-2418	20040610
		EP 2002-784436	20021026
		WO 2002-US36213	20021026
TW 2003001134	A	TW 2002-133208	20021113

FILING DETAILS:

PATENT NO	KIND	PATENT NO
BR 2002014168	A Based on	WO 2004039826
AU 2002346369	A1 Based on	WO 2004039826
EP 1562968	A1 Based on	WO 2004039826

PRIORITY APPLN. INFO: WO 2002-US36213 20021026; US
2001-332437P 20011114; US
2001-332743P 20011114; TW
2002-133208 20021113

AN 2004-419571 [39] WPIDS

AB WO2004039826 A UPAB: 20040621

NOVELTY - A chimeric, humanized or CDR grafted antibody or its fragment capable of inhibiting human IL-6 comprising at least one heavy or **light chain** complementarity determining region (CDR) derived from the anti-IL-6 murine monoclonal antibody CLB-8 and a constant region derived from one or more human antibodies, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) an isolated IL-6 antibody encoding nucleic acid;
- (2) an isolated IL-6 antibody or its specified portion or variant comprising the antibody in (1);
- (3) an IL-6 antibody encoding nucleic acid composition comprising the nucleic acid, and a carrier or diluent;
- (4) an antibody vector comprising the nucleic acid;
- (5) a host **cell** comprising the isolated nucleic acid;
- (6) **producing** at least one IL-6 **antibody** or its specified portion or variant;
- (7) an IL-6 antibody composition or specified portion or variant composition comprising the IL-6 antibody or specified portion or variant, and a carrier or diluent;
- (8) treating an immune disorder or disease in a **cell**, tissue, organ or animal;
- (9) modulating at least cancerous disorder or condition in a **cell**, tissue, organ or animal;
- (10) a medical device comprising at least one of the antibody cited above;
- (11) a formulation comprising at least one IL-6 antibody or specified portion or variant, and at least one selected from sterile water, sterile buffered water, or at least one preservative;
- (12) treating at least one IL-6 mediated condition by administering the formulation to the patient;
- (13) an article of **manufacture** for human pharmaceutical use comprising packaging material, and a container comprising a solution or a lyophilized form of at least one IL-6 **antibody** or its specified portion or variant;
- (14) preparing the formulation; and
- (15) a transgenic animal or plant expressing at least one of the antibody.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antirheumatic; Antiarthritic; Osteopathic.

No biological data given.

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